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CONTENTS

Fundamental Research in the Clinical Specialties: *V. Everett Kinsey* 373

Environment and Food Intake in Man: *Robert E. Johnson* and *Robert M. Kark* 378

The Terminology of Pollination: *J. R. King* and *R. M. Brooks* 379

News and Notes 381

Comments by Readers 386

Technical Papers

The Effect of Body Temperature on the Duration of Barbiturate Anesthesia in Mice: *Frederick A. Fuhrman* 387

Hyperheparinemia: Cause of the Hemorrhagic Syndrome Associated With Total Body Exposure to Ionizing Radiation: *J. Garrott Allen* and *L. O. Jacobson* 388

Treatment of Plutonium Poisoning by Metal Displacement: *Jack Schubert* 389

Effect of Temperature on the Growth and Sterility of Maize: *Donald F. Jones* 390

Failure of Sodium Salicylate to Inhibit Hyaluronidase *in Vitro*: *Robert M. Pike* 391

The Carcinogenic Action of Smegma: *Alfred Plaut* and *Alice C. Kohn-Speyer* 391

In the Laboratory

A Simple Laboratory Apparatus for the Demonstration of Cardiac Ballistics: *Vernon E. Krahl* 393

Control of *Nosema* Disease of Potato Tuber Worm, a Host Used in the Mass Production of *Macrocentrus ancylivorus*: *H. W. Allen* and *M. H. Brunson* 394

A Single Flashlight Source for Ultracentrifuge Research: *Lionel L. Lipschultz* and *Kurt G. Stern* 395

An Apparatus for the Determination of the Tensile Strength of Healing Wounds: *Jesse Charney, Martin B. Williamson,* and *Finn W. Bernhart* 396

Book Reviews

Analytical method in dynamics: H. O. Newboult. Reviewed by *Henry Margenau* 398

Scientific Book Register 398

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Fundamental Research in the Clinical Specialties

V. Everett Kinsey

Howe Laboratory of Ophthalmology, Harvard Medical School, and Massachusetts Eye & Ear Infirmary, Boston

THE SUCCESSFUL OUTCOME OF GOVernment-supported research during the war has focused the attention of the public as well as professional groups on the desirability of continuing a part of this activity. Bills to provide funds for research in various branches of science are now before Congress. That these bills have not passed perhaps reflects the divergence of opinion of scientists on the details of administering potential funds rather than the temper of the people on the question of public support of research. It seems possible, therefore, that in the future Congress may appropriate funds for general research purposes. Although lack of funds is one of the chief factors limiting additional research, a comprehensive plan by which expansion may be carried out is just as essential as ample financial support.

In order to determine the present status of fundamental research in the clinical specialties and the readiness of clinical laboratories for expansion when more adequate financial support is provided, the writer has visited a number of medical schools. In general, the impression was obtained that research teams adequate to cope with the fundamental problems in clinical medicine are few. This was confirmed by many of the clinical men interviewed, who expressed dissatisfaction with the present lack of teamwork between clinician and scientist in basic research.

Among the points studied particularly in arriving at this conclusion were: (1) the organizational methods by which research is conducted; (2) the magnitude of the research; and (3) the extent to which the needs of the particular clinical specialty are fulfilled.

Only the larger university medical schools were visited, since it might be presumed that fundamental research would be conducted in these universities on as large a scale as anywhere in the United States. The schools were located along the Atlantic Seaboard, in the Middle West, and on the Pacific Coast.

Typical of the conditions discovered is the situation in a clinical department of one of the midwestern universities. The head of this department is well known in his field. Clinical facilities appeared to be excellent, and space is available for making experimental studies. However, since the termination of a large grant five years ago no full-time investigators have been employed. Members of the clinical staff go to the laboratory occasionally and conduct occasional experiments as a part-time activity. No men from departments of basic science, such as bacteriology or biochemistry, have been assigned to work in the department. Plans have been made to obtain a research director who would be expected to devote half time to coordinating studies made in the department, a quarter to private practice (the income from which would comprise a significant fraction of the research budget), and the remaining quarter to work of his own choice.

Another instance which is not typical but which illustrates the consequences of halfway measures is the situation in a department located in a teaching hospital in a large medical school in the East. The department head is a clinician who previously gained an international reputation for his research work. Unlike that of most men in this position, his salary is adequate to allow him to devote full time to the department—in fact, the position was especially created so that he might have more opportunity for institutional activity, particularly for the "luxury" of research. When asked whether, under these apparently favorable circumstances, the research in his department was developing satisfactorily, his unhesitating answer was "no." Although he believed that the provision for full-time academic work was a step in the right direction, he estimated that 90 per cent of his time was taken up with such administrative duties as obtaining new house officers, making rounds, settling petty squabbles, and numerous other details requiring the attention of a department head. Moreover, research by others on the staff is sporadic; an excellent young investigator was recently forced to enter private practice to make a living wage. The only full-time studies being conducted at present are carried out by a single investigator, a chemist.

In the two departments described definite efforts have been made by capable administrators to conduct research programs within the departments, but these have failed in their objective because of lack of funds. In departments in other institutions visited, no fundamental research has been attempted, and no facilities or personnel are available.

A method of conducting research which is being used increasingly is to assign members from departments of basic science to the clinical department or vice versa. Salaries and duties are divided. In a few instances this method has proved successful; more often the complaint is heard that the clinical man is unsympathetic with the choice of problem and that little actual contact exists between the basic scientist and the clinician, who spends most of his time in private practice. A variation of this

arrangement is for the clinician to consult, either by periodic conference or when the occasion arises, with men in the preclinical departments. With the exception of one institution, where periodic conferences were implemented with laboratory work performed by full-time investigators, it was evident that this arrangement produced little more than conferences. The principal weaknesses of the conference method lie in the lack of mutual understanding and time, existence of other interests, and minor annoyances encountered in a joint investigation with busy co-workers frequently located on the other side of town.

Some research in clinical specialties is done in the basic science departments; these researches frequently lack continuity and are often of an analytical nature. As such, they are of great value. However, the mere accumulation of facts is not sufficient; it is important, in addition, *to use them to establish new principles* or to confirm old ones. This is an endeavor which requires background and insight both in the basic sciences and in the clinical field in which known facts are to be used.

In addition to research in medical schools and associated hospitals, an increasing number of studies, particularly in medicine, are being conducted in research institutes and industrial laboratories. Despite obvious limitations, the majority of these are well organized and are performed by trained full-time workers. The clinical testing for both groups must be farmed out to nearby hospitals.

It is impossible to obtain an over-all picture of fundamental research in medicine without taking into account the increased emphasis placed on studying separately such diseases as cancer, tuberculosis, poliomyelitis, arthritis, and those affecting the heart. While these diseases are also the concern of different clinical specialties, they represent single entities, and the study of each is likely to become a specialty.

The number of people working in a given field is small indeed. This is illustrated by an example chosen from the specialty with which the writer is particularly acquainted, namely, ophthalmology. Glaucoma is caused by excessive intraocular pressure, which if untreated, results in blindness through excavation of the optic nerve head. This disease is the chief cause of irrevocable blindness in individuals past middle life and is typical of the dramatic type of illness which might be expected to stimulate research. How many investigators in the United States are devoting half or more of their time to studying glaucoma? Or, more important, how many are investigating basic physiological processes in the eye which might lead to a successful therapy? A generous estimate is *three*.

It is concluded from the information obtained that many halfway measures are being employed in an attempt to carry out research programs in the clinical specialties. As a result, the amount of fundamental research in the clinical field is extremely small in comparison with that in the preclinical sciences. Of the persons interviewed, all but one is dissatisfied with the present state of investigational activities in his field, the exception being a man ready to retire. The implied excuse for this deficient state is a lack of funds available over an extended period. Not only is basic research undeveloped in these fields of medicine, but it is apparent that if sufficient funds to carry out an intensive research program were immediately forthcoming, few departments have any trained personnel or well-laid plans for their effective use. This condition can be attributed in part to a defeatist attitude born of previous unsuccessful attempts to overcome the multiple difficulties inherent in combining an extensive research program with teaching and running a successful clinical department. It seems appropriate, therefore, to consider measures which might remedy this situation.

Program for Expanding Research

One way to expand research is to increase the number of laboratories investigating specific diseases. The inherent emotional appeal and the ease with which such programs can be delineated are strong tactical arguments in favor of this method. The disadvantages, particularly with small projects which may be forced to advertise their progress, are less apparent but just as real. There is danger, for example, that the interests of research workers may become narrow, that promising leads in the solution of other problems cannot be exploited, and that the feeling of constant pressure to turn up a "cure" may stimulate "long-shot" experiments at the expense of sound but more methodical investigations.

Another means of furthering research in clinical specialties is to establish research institutes in which investigations relating to a number of specialties could be performed. This method offers no appreciable advantage over the one to be recommended and entails considerable duplication of existing facilities and personnel.

A sounder plan, which does not call for significant changes in administration or physical layout, is to establish laboratories staffed with well-trained, full-time workers in the clinical departments of university medical schools. The objective is to develop the fundamental aspects of the clinical specialty and make these available to the postgraduate student. This method is not novel, since it has been successfully carried out over a period of years in the Howe Laboratory of Ophthalmology. Experience gained in this laboratory should be useful in considering a more widespread application of this method.

Historically, there has been little precedent for full-time investigators in clinical specialties; however, the tremendous developments in the basic sciences have suggested many new approaches to the solution of medical problems. These have complicated inordinately the methods of doing research. Whereas in the past many studies leading to fundamental discoveries have been

made by isolated workers devoting their leisure time to research, present-day experience indicates that most progress comes from the cooperative effort of individuals having different training and background. Research of this kind is essentially a full-time job if facilities and personnel are to be utilized efficiently and if the quality of the work is to compare favorably with that in other branches of science.

The Laboratory for Fundamental Research

The first step in establishing a research laboratory is to secure the services of an able director. At first thought it may appear that the head of the clinical department should also be the director of the research laboratory. This is inadvisable, however, because: (1) directing a laboratory is a full-time job; (2) the person in charge of a clinical department is usually interested chiefly in the practice of medicine rather than in basic research; (3) the head of a clinical department frequently lacks the scientific background which would qualify him to direct research; (4) the clinical professor may be inclined to encourage studies with immediate practical application rather than those of a more fundamental nature; and (5) the demands of his practice would pre-empt both the time and attention of the clinical professor. Actually, both positions are of such importance and involve functions so separate that a parallel rather than a vertical administrative organization is desirable.

The qualifications of the laboratory director should include a sound basic training in either medicine or science, a broad general interest and background in research, and, if possible, administrative experience. It is of greatest importance that the director be wholly in sympathy with the idea of a laboratory in which appropriate problems in basic science are investigated for the purpose of advancing a medical specialty.

A competent staff is no less important for the laboratory. Before selecting a staff it is necessary to recognize that its primary function is to conduct studies of a fundamental nature, not merely to be concerned with case-history reports, statistical studies, and the delineation of techniques.

In recent years advances in clinical medicine have paralleled great developments in the basic sciences. The growth of knowledge in both fields has been so extensive that to become a clinician, a physiologist, or a bacteriologist is a major achievement. Few individuals receive additional training or possess experience outside a single specialty. Accordingly, since the purpose of the research organization is to employ the concepts and techniques of the fundamental sciences in the investigation of problems in clinical medicine, it is essential that the staff include some individuals trained in preclinical sciences and others trained in a clinical specialty.

Each member of the staff should be prepared to conduct independent research and to work on equal terms in cooperative investigations whenever this is to mutual advantage. This type of organization assures that the scope of the work will be more broadly representative of the specialty, permits greater flexibility in the choice of problems, and takes advantage of the combined talents of the staff as a whole. That these talents consist of more than technical skill is not always appreciated. For example, the function of the preclinical scientist in research is frequently assumed to be merely that of a "glorified" technician. This was illustrated recently by the comment of a man who wanted to promote research in his clinical department. He said that what he "really wanted" was a biochemist who could perform analyses, the implication being that the success of a well-developed research program depends exclusively upon the performance of analytical work. In this kind of thinking, emphasis is on the results of analysis and not on the fundamental concepts which are prerequisite to intelligent interpretation. To this man, who is representative of many well-known clinicians of the older school, a person trained in the basic sciences is merely an adjunct to the laboratory whose scientific acumen is disregarded entirely and whose technical services are overrated. In this instance, the mistake is not in obtaining a biochemist but in misunderstanding completely his function in the laboratory. Therefore, to utilize the basic scientist fully it is essential that, in addition to using his technical skill, his intellectual capacities and talents be directed toward the conception and solution of research problems.

Following the same reasoning, the knowledge which clinically trained men possess concerning normal and disease processes should be applied to the solution of basic problems as well as to those of clinical significance.

The recommended individual approach to experimental problems may not appear possible in view of the limitations of specialized training already discussed. Actually, this may be true, but only during the initial stages of development. One of the chief attributes of an organization of this type is the day-to-day association of scientists and clinicians which eventually leads to mutual understanding of both fields. This, in turn, develops in each worker the ability to think in terms of both the clinical and scientific aspects of a problem. It is only when this point is reached that each member of the group is able individually to pursue effective independent research, and the laboratory as a whole is competent in all major phases of a specialty.

A secondary function of the staff is postgraduate teaching of basic science applied to a medical specialty. The laboratory staff should have the same teaching relation to the clinical specialty as the staff of the preclinical department has to medicine as a whole. For example, physiology might be limited to physiology of the eye or the urinogenital system, as the case may be. Experience in different branches of the specialty pre-eminently fits the laboratory staff for this task. It may also be desirable

for the staff to assist in postgraduate teaching in clinical subjects, but all teaching should be so arranged that it does not occupy over approximately a quarter of the staff's time; in any case, it should not be permitted to bring research to a standstill.

The number on the staff will vary with the physical facilities of the department and with the financial support, but three is probably a minimum number for an effective unit, and four or five is better.

A laboratory staff in neurology, for example, might include two clinicians having different research interests, a physiologist, an anatomist, and a biophysicist. Arrangement should be made so that other members of the clinical department and investigators who might be assigned from cooperating preclinical departments could also participate. Temporary associates supported by term grants could assist the research group. Adequate technical assistants, secretarial aid, and an animal room attendant should also be provided.

If the laboratory unit is to function effectively, and if mistakes which in the past have resulted frequently in scanty and mediocre research are to be avoided, special consideration must be given to academic standing, remuneration, and tenure of the staff.

The system of rank in most clinical departments differs significantly from that in preclinical departments. It is customary in the former to have a professor, one or more assistant or associate professors, and a much larger number of assistants and instructors. In most instances the latter devote but a small fraction of their time to teaching and little or no time to research; they may continue without advancement in rank for life. Many of the men holding these lower ranks are outstanding physicians in the community, and their reputations are independent of their academic rank in the medical school.

In the preclinical departments, on the other hand, the staff ordinarily is much smaller and consists chiefly of men who devote full time to academic work. The same system of rank prevails, but the assistants, instructors, and usually assistant professors are young men. For them, rank determines their standing in the profession.

Since the staff of a fundamental research laboratory consists of career men, their academic status should be comparable with that of career men in other academic fields rather than with that of their co-workers in clinical medicine. In order to describe more accurately the type of work performed and to avoid the appearance of discrimination, it is preferable that the titles of the laboratory staff be different from those of the clinical staff, e.g. professor of neurological research, on the one hand, and professor of neurology, on the other.

The income of men in research does not approach that of the average practicing physician. If qualified physicians are to be attracted to medical research, a reasonable salary and satisfactory security in tenure is essential, particularly if they are to remain in this vocation. Salaries must compare favorably with those offered in basic science departments and in industrial research laboratories.

In such matters as academic standing, remuneration, and tenure the policy of the research laboratory may well be patterned after that of the preclinical rather than the clinical department. In problems of organization, on the other hand, this is not true because of distinct differences in personnel. For example, the staff of a biochemistry department ordinarily consists solely of biochemists, that of a bacteriology department only of bacteriologists, etc. In contrast, the complexity of fundamental research in the clinical field requires a staff of individuals from various fields. Strict adherence to the vertical system of departmental organization common in academic departments is unsuitable for the small staff of the laboratory. This is not to say that the usual academic advancement through the ranks should be abandoned, but to point out that as each staff member becomes, through experience and accomplishment, an authority in his own right, he should be rewarded with the rank and salary that he might have had if he had remained in his original specialty.

With rising costs, a budget for a laboratory involves some uncertainty. However, approximately $12,500 to $15,000 per year per staff member is probably a good estimate. This amount should cover salaries for the staff, technicians, secretaries, diener, and machinist, and the cost of animals, supplies, and equipment. A laboratory consisting of four staff members would require between $50,000 and $60,000 per year.

It is pertinent now to discuss several less tangible matters of importance in establishing research laboratories in the medical specialties. First, if the basic scientist devotes sufficient time and effort to becoming familiar with both the medical and scientific aspects of a specialty, it is possible that he may not be able to maintain in each the same proficiency as the more specialized individual. It has been said that he is neither fish nor fowl. This criticism might well have been made about the biologist or chemist who first transcended the horizons of his specialty to become a "biochemist," but few would deny that this "hybrid" has contributed more to the development of biochemistry than has the biologist and the chemist. The great contributions to the advancement of knowledge in the scientific aspects of medicine may well come from another "hybrid" who might be called the "medical scientist."

Secondly, in leaving an established field such as clinical medicine or basic science to work in a relatively new, composite field, the staff may experience a degree of professional isolation. If the laboratory is located in a hospital away from preclinical departments, this feeling of isolation is likely to be more acute in the basic science.

It may be reduced by more positive recognition from the clinical staff of the department, by association of the basic science group with members of the preclinical departments, and by the formation of professional organizations created for workers in the special field. Membership in most medical groups is limited to those with a degree in medicine. Since the prime reason for this limitation concerns the practice of medicine, which is not involved, some special status in the local or regional organization covering the specialty should be created for the nonmedical members of the laboratory. This would be mutually advantageous, since it offers opportunities for professional contact and provides means by which clinical members may keep abreast of recent developments in the more fundamental aspects of their specialty.

As interest in fundamental research in the clinical specialties increases, societies for the exchange of papers, and possibly special journals, provide other ways of reducing the isolation. The trend in this direction is illustrated in ophthalmic research by the formation of the Association for Research in Ophthalmology, Inc., and by plans for a special technical section in an ophthalmological journal.

Scope of the Program

The number of laboratories necessary to bring fundamental research to a state of development comparable with that in other branches of science is dependent upon the number of clinical specialties involved, the proportion of total investigational activity in the fields for which these laboratories might assume responsibility, and the special requirements of any given specialty.

Although departments representing every clinical specialty were not visited, a definite need for increased basic research was expressed in the following fields: dermatology, medicine, neurology, ophthalmology, orthopedics, otolaryngology, pediatrics, and urology. Since several others might be added to this list, a total of 10 specialties is a reasonable estimate.

It is beyond the scope of this paper to discuss the research needs of all of the specialties or to attempt a close estimate of the proportion of the total research in any one of these fields which ultimately might be performed in these laboratories. However, in ophthalmology four such groups might well be organized. If this specialty is reasonably typical of the average, the number of research laboratories in all of the fields would be of the order of 40. On the basis of the budget previously given, this would call for an annual expenditure of approximately $2,500,000.

Immediate Objectives

The financial requirements of the proposed program may appear to present insurmountable difficulties to any action which could be taken without government support. Furthermore, because of the undeveloped and unorganized state of basic clinical research, it would be premature to attempt to put into operation so comprehensive a program or, indeed, any alternative plan comparable in scope without a preliminary test on a smaller scale. To this end, steps should be taken now to set up one research group in each of four specified clinical fields to serve as nuclei around which expansion could be planned. These four laboratories would cost approximately $250,000 per year and should be planned for a minimum period of 8 years, making a total expenditure of about $2,000,000. They need not be located in the same university, but the existence of a central authority to coordinate the whole effort and maintain unity of purpose is essential. In operating these test laboratories information would be obtained concerning the effectiveness of this method of conducting research which might well transcend in importance the scientific results. However, the latter alone should more than compensate for the effort made.

Provision should be made at specified intervals to evaluate progress in these laboratories. This evaluation and plans for enlarging the program might be made by the sponsor in cooperation with an independent board created for the purpose.

The immediate questions are: What means are available for establishing four initial laboratories, and who would be responsible for such action? It might appear that government support is the logical answer. However, except in those fields of interest which fall within the domain of the War or Navy Departments or the Division of Public Health, few governmental funds are yet available for general distribution to medical laboratories. Since the research interest of the proposed program does not coincide with that of these government agencies, private support must be obtained. This is not without its advantages, as the greater flexibility and altruism permitted by private foundations are especially valuable during the formative period of a new venture.

In general, funds may be sought from three main sources: private individuals, public subscription, and foundations. They may be in the form of outright endowment or periodic contributions.

Appeals to private individuals and the public have proved successful in obtaining funds for studying cancer, poliomyelitis, and tuberculosis. There are two drawbacks to the use of this method for establishing the four test laboratories. First, an appeal to the public requires a highly organized campaign which depends on a previously existing organization; secondly, since most laymen and many nonlaymen do not understand the broad aims of fundamental research, the response is likely to be poorer than it has been when money was solicited for investigation of specific diseases.

There are numerous foundations whose purpose it is to further medical research. The history of medical education and research relates many instances in which the

successful inauguration of a new venture depended upon receiving financial support from a foundation. The proposed program probably is no exception. However, its financial needs pose new questions to the foundations, for large sums are required over an extended period. In the past, most foundations have given only relatively small sums for specific projects and for periods rarely exceeding five years. The prospect of obtaining the requisite funds for establishing fundamental research laboratories in clinical medicine may depend upon the degree in which the foundations will allow precedent to influence their present policy. Whereas this policy may well have been a wise one in the past, an eminent authority, Dr. Alan Gregg, in *The furtherance of medical research* (1941), has advocated that "the larger foundations return to making capital grants for endowment and for both the larger and the smaller foundations to make fewer grants for terms of seven to twelve years instead of one to three." In so far as these viewpoints are accepted by the foundations and point to a trend in their policy, it is to be hoped that aid from them to expand fundamental research in clinical medicine will be forthcoming, at least until the public feels obliged to assume the responsibility for the support of research and thus makes it possible for the scientist to devote himself to science and not to raising funds.

The responsibility for *initiating* significant expansion of basic research in clinical medicine and for formulating a program worthy of support from the foundations or the public rests primarily with those forward-looking clinicians and basic scientists who realize that continued progress in medicine depends upon the discovery of new basic principles.

Environment and Food Intake in Man

Robert E. Johnson[1] and Robert M. Kark

Harvard Fatigue Laboratory, Soldiers Field, Boston

ALTHOUGH IT HAS BEEN ASSUMED THAT feeding habits among men are modified by differences in climate (*4*), very few quantitative, reliable studies have been reported on the effects of different environments on the voluntary food intake of men doing the same type of work.

Between 1941 and 1946 reliable data have been collected on the average day's food which healthy, physically fit soldiers (ground troops) chose to eat from the rations provided in temperate, mountain, desert, jungle, arctic and subarctic areas in North America, Europe, and Asia. Most of these data were obtained during surveys and Army ration trials conducted intermittently throughout the war. Calculations were made according to the method of Berryman and Chatfield (*1*).

The present communication is taken from a critical review of the nutrition of United States and Canadian soldiers prepared in 1946 for the U. S. Army by Johnson and Kark (*3*). Fig. 1 and Table 1 show some data on the nutrient intake of healthy, physically fit, young North American soldiers who lived and fought in different environments in different parts of the world. Each point in Fig. 1 represents the average caloric intake for groups of from 50 to 200 men who, at the time of examination, were fully acclimatized to the particular environment in which they were living and who showed no signs of nutritional deficiency. For the purposes of this discussion, data have been selected only from groups of men who were receiving an ample ration in wide variety and of such quantity that they could have eaten more if they had wished to do so. This ideal situation in the feeding of troops was, unfortunately, not always achieved. The data show a striking correlation between the average voluntary daily caloric intake and the mean environmental temperature to which the groups of men were exposed. The range was

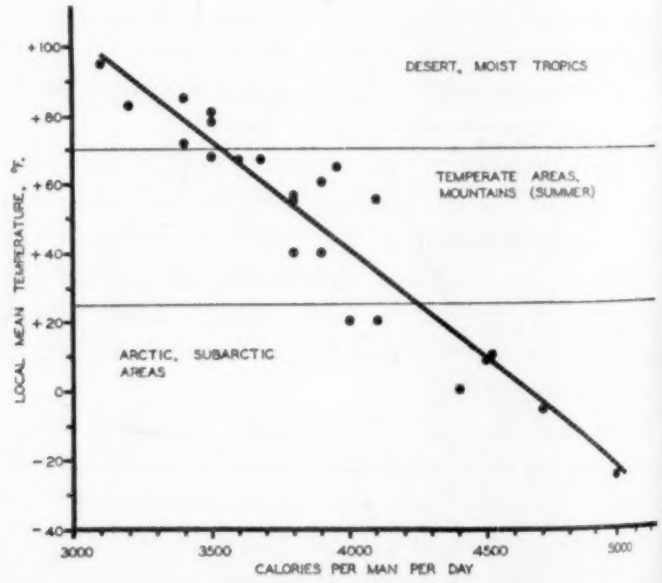

FIG. 1. Voluntary caloric intake, North American troops (averages for groups of 50 or more men).

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The subject matter of this paper has been undertaken in cooperation with the Committee on Food Research of the Quartermaster Food & Container Institute for the Armed Forces. The opinions or conclusions contained in this report are those of the authors. They are not to be construed as necessarily reflecting the views or endorsement of the War Department.

from 3,100 calories in the desert (92°F.) to 4,900 calories a day in the Arctic (−30°F.). This very large difference in caloric intake cannot be explained in terms of changing basal metabolic rates (*2*), which vary at the most by 20 per cent between arctic (Greenland) and tropical (Java) environments (equivalent to only 400 calories/24 hours); nor can it be explained in terms of difference in body size (Table 1) or in terms of different activities, since the ground troops carried out much the same tasks in all environments. We have no crucial evidence to decide this latter point, but we believe that the caloric expenditure for a given task is greater in cold than in warm climates because of the hobbling effect of arctic clothing and equipment. In addition, more heat is required in cold than in warm environments to maintain thermal equilibrium.

TABLE 1

BODY WEIGHT, CALORIC CONSUMPTION, AND RATIO OF PROTEIN, FAT, AND CARBOHYDRATE EATEN BY REPRESENTATIVE GROUPS OF GROUND TROOPS IN DIFFERENT ENVIRONMENTS

Place and troops	Environment	Average body weight (kg.)	Average caloric intake/man/day	Percentage of calories provided by:		
				Protein	Fat	Carbohydrate
Canada, mobile force "Musk Ox"	Arctic and subarctic	73.0	4,400	11	40	49
U. S. A., ground troops	Temperate	69.0	3,800	13	43	44
Colorado Rockies, infantry	Temperate mountain (9,000 ft.)	69.5	3,900	13	34	53
Pacific Islands, ground troops	Tropics	70.0	3,400	13	33	54
Luzon, infantry	Tropics	65.5	3,200	12	34	54

Table 1 demonstrates that, regardless of environment, the percentage of proteins voluntarily chosen from the rations was practically constant in all environments, and that even in the tropics the percentage intake of protein and fat was "high" by traditional criteria and not much different from what it was in the Arctic.

The chief practical implications of these data are that the same general types of rations can be provided for ground troops regardless of environment, whether cold or hot, and that greater quantities of food are needed to feed men in cold weather than in hot.

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The Terminology of Pollination

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PLANT BREEDERS INTERESTED IN pollination work realize the variations relative to the application of the terms designating the expressions of pollination. It is not the purpose of this brief discussion to draw conclusions at the present time or to offer a cure for the ills which will be apparent, but simply to present facts.

The common conception of pollination in the angiosperms is the transfer of pollen from the anther to the stigma of a flower. There are, of course, exceptions to this general conception. For example, in horticultural usage alone, particularly with reference to orchard fruits, the term is sometimes applied in a general way to designate all the influences concerned in the setting of fruit; or pollination may be concerned with both the transfer of the pollen to the stigma and its subsequent germination thereon; while again, both pollination and fertilization have been used synonymously to imply application of pollen to the stigma. We are concerned with a brief presentation of the variability in use of the most common terms—self, close, and cross—used in delimiting the process of pollination, rather than with a discussion of the numerous terms which designate the ramifications of these general expressions and are based upon the great variety of structures and mechanisms among flowers.

Much confusion has been brought to the common conception of pollination as a transfer of pollen from anther to stigma, because structural, genetic, and mechanical aspects of the phenomenon have all been considered. This state of affairs pertains more to the common terms, such as self, close, cross, and closely applied terms which designate general types of pollination, than to specialized terminology as exemplified by the classifications of Knuth (*Handbook of flower pollination*, Vol. I, 1906). Horticulturists and botanists in general seem to differ as to the exact definitions of the

terms self- and cross-pollination, usually defining them from a "mechanical" viewpoint, namely, a transfer of pollen. But in their *use* of the term the ideas of structure and genetics are brought in which extend this conception *beyond* the single act of transfer.

From one point of view, self-pollination is the transfer of pollen from the anther of a flower to the stigma of the same flower, and cross-pollination is pollination between the anthers and stigmas of different flowers on the same plant or between flowers on different plants of the same variety or different varieties. From another viewpoint, it would be considered that self-pollination is the transfer of pollen from one flower to the stigma of the same flower, to the stigma of another flower on the same tree, or to the stigma of a flower on another individual of the same variety. Likewise, in this sense, cross-pollination would involve the pollen of one variety and the pistil of another. Pollination within both monoecious and dioecious forms of the same variety or species would always be self-pollination, from one viewpoint; while dioecism would always be, and monoecism would sometimes be, cross-pollination in a typically different viewpoint. Only intraspecific pollination is reviewed here, since interspecific pollination is considered as cross-pollination in all cases.

Although these two general viewpoints are in evidence, the situation is confused by the continued appearance of definitions and usages of the terms self- and cross-pollination, which suggest different degrees of variation between the above two delineations. For example, self-pollination is the conveyance to the stigma of pollen from the anthers of the same flower or from a flower on the same plant, while cross-pollination involves pollen from a flower on another plant of the same or a different variety. Again, self-pollination is the transfer of pollen from the anther of a flower to the stigma of the same flower, while cross-pollination takes place between flowers of the same plant, or between flowers of different plants of the same variety.

Close-pollination has been frequently referred to in conjunction with self-pollination and, likewise, has also assumed different meanings. Whereas self-pollination is limited completely to an individual flower, close-pollination designates pollination involving different flowers on the same plant; yet again, exactly the reverse definition has been given. Close-pollination may also be extended by the same worker to mean pollination which takes place within an individual flower, between flowers on the same plant, or between flowers on the same plant and flowers on different plants of the same variety. Self- and close-pollination are also used synonymously in relation to the complete occurrence taking place within an individual flower. The term close-pollination has likewise been used to refer to the fact that in some plants pollination occurs before the buds open. Lastly, the term "self" may not be used at all, being replaced entirely by "close," which refers in such cases only to pollination between the anther and stigma of the same flower while cross-pollination refers to all other forms.

Open-pollination is used frequently in horticultural literature in a very broad sense to include uncontrolled pollination between anthers and stigmas, irrespective of their relations to each other—that is, whether they are in the same flower or in different flowers of the same or different variety. This term, therefore, is intended to be used in relation to artificial pollination as contrasted to natural pollination, and hence should not be included in the types discussed in preceding paragraphs. To do so would confuse the issue still more. Interpollination is used less frequently, and has been designated as pollination between closely related species or subspecies or between flowers of a cluster on the same plant.

In spite of the general confusion in terminology, the phenomenon could be considered from any of three viewpoints:

(1) Pollination defined in its original form as the transfer of pollen from an anther to a stigma would not necessitate the designation of the relative positions of anthers and stigmas. If it is considered in this manner, the single term *pollination* would adequately describe all types.

(2) The terminology could be enlarged to distinguish between the transfer from anther to stigma in the same flower and from the anther of one flower to the stigma of another, regardless of any hereditary relationship between flowers concerned. On this basis, the two terms *self-* and *cross-pollination*, respectively, would serve.

(3) However, we might take into account not only pollination within an individual flower and between different flowers, but also whether these different flowers are of the same clone, the same strain, the same variety, or the same subspecies or species. This would necessitate four major categories of pollination instead of one or two: (1) within an individual flower, (2) between flowers of the same plant, (3) between flowers of different plants of the same variety (where varieties are recognized) or species, and (4) between flowers which are on plants belonging to different varieties (either clonal or pure line) or species. In regard to (3), distinctions must be made between plants of (a) a variety whose population is made up of clones, such as the horticultural clones of pear, peach, apple, almond, and the like, and (b) a variety whose population is composed of sexually propagated individuals, such as many floricultural plants (aster, sweet pea).

Although it is known that inconsistencies do exist in the conception of what constitutes the different expressions of pollination, the extent of such inconsistencies is perhaps not fully realized. If we have done no more than present this situation and the facts in a more organized manner, this discussion has served its purpose.

NEWS *and Notes*

The Association regrets to inform the readers of *Science* that on April 5, 1947, Dr. Willard L. Valentine, editor of the journal since January 1, 1946, died at his home from sudden heart failure.

Prior to assuming the editorship of *Science* Dr. Valentine was chairman of the Department of Psychology at Northwestern University. He is survived by his wife, Norma, and two children, Richard and Virginia. Funeral services were held in Columbus, Ohio, on April 8.

About People

Richard Foster Flint, professor of geology at Yale University, will present a series of three illustrated lectures on the general subject of "The Glacial Ages" at the Wagner Free Institute of Science, Washington, D. C. The lectures are entitled: "Glaciers of Today and Yesterday" (April 11), "Indirect Effects of Glaciation" (April 12), and "Glacial and Interglacial Climates" (April 18). The lectures will begin at 8:00 P.M., and admission will be free.

A. Earl Pritchard, U. S. Public Health Service Communicable Disease Center, has been appointed assistant professor of entomology and assistant entomologist in the Experiment Station, University of California, Berkeley.

James M. Schopf, paleobotanist, U. S. Bureau of Mines, has been granted leave to conduct a special study of South African coal under auspices of the South African Council of Scientific and Industrial Research, with headquarters at the South Africa Geological Survey, Pretoria. Dr. Schopf will return to this country early in October.

C. Stacy French, associate professor of plant physiology, University of Minnesota, Minneapolis, has been appointed director of the Division of Plant Biology, Carnegie Institution of Washington at Stanford University, California, to begin July 1. He will succeed H. A. Spoehr, chairman of the Division since 1932, who will devote full time to research on production of carbon compounds by plants.

Dr. French joined the Minnesota faculty in 1941. His research has been concerned with cellular respiration, the photosynthesis of purple bacteria and green leaves.

E. Raymond Hall, director, University of Kansas Museum of Natural History, returned March 20 from the University of Costa Rica Museum of Natural History after a month's study.

A. S. Pearse, professor of zoology, Duke University, was feted at dinner by over 60 biologists on his 70th birthday, March 14. He was presented with a bound volume of letters from former students.

Herbert M. Evans, director, Institute of Experimental Biology, University of California, delivered the 23rd Ludvig Hektoen Lecture of the Frank Billings Foundation, Institute of Medicine of Chicago, Friday evening, March 28. His subject was: "The Internal Secretions of the Pituitary Body."

Albert R. Mead, research fellow in zoology, University of California, Berkeley, has been appointed instructor in zoology, University of Arizona, Tucson.

Visitors to U. S.

Joel Axelsson, Institute for Utfodringslara, Uppsala, Sweden, is conducting research on the digestibility of feeds with Burch H. Schneider, Agricultural Experiment Station, West Virginia University, under a fellowship from Swift and Company, Chicago.

Maurice Stacey, University of Birmingham, England, will be guest of honor at sessions of the Division of Sugar Chemistry and Technology, American Chemical Society, at meetings in Atlantic City, April 15–17. On April 16 Prof. Stacey will participate in a symposium on sugars and amino sugars in biochemistry.

Gregory Wentzel, professor of theoretical physics, University of Zurich, is at present a visiting professor at Purdue University, Lafayette, Indiana.

A. J. Petrick, acting director, Fuel Research Institute, and **J. W. van der Merwe,** assistant industrial adviser, Department of Commerce, South African Government, arrived in this country early in March to study developments in synthetic liquid fuels production from coal.

Fellowships

Cornell University School of Nutrition announces the following fellowships for 1947–48: two Philco frozen food fellowships of $1,300, one for studies on cooking and another on processing frozen foods; and two $1,500 Robert Gould research fellowships in nutrition. Applicants must hold the Bachelor's degree and be otherwise qualified for admission to the School. Information may be obtained from the Office of the School of Nutrition, Cornell University, Ithaca, New York.

Grants and Awards

The 1947 Franklin Medal, highest honor of the Franklin Institute, Philadelphia, will be awarded to Enrico Fermi, Nuclear Research Institute, Chicago, and Sir Robert Robinson, professor of chemistry, Oxford University, England, at Medal Day exercises in Philadelphia April 16.

Dr. Fermi will receive the honor for outstanding work in the field of atomic energy. "His immediate recognition in 1932 of the neutron as an atomic projectile has resulted in much of what science knows today of this important development," the Institute stated. For this work he received the Nobel Prize in physics in 1938.

Sir Robert Robinson will be honored for contributions to the present knowledge of natural substances, particularly contributions in the sterol field and work on pyrimidine analogues and their relation to vitamin B. He was knighted in 1939 for contributions in the field of organic chemistry.

The gold medal, carrying a medallion of Benjamin Franklin, is awarded annually to workers, regardless of country or creed, who have done most to advance a

knowledge of physical science and its application.

Charles Allen Thomas, vice-president and technical director, Monsanto Chemical Company, St. Louis, and president-elect of the American Chemical Society, was named as the second recipient of the Industrial Research Institute Medal at the close of the Institute's winter meeting in Chicago, February 27–28. Formal presentation of the award, which is granted for an outstanding contribution to industrial research, will be made at the annual meeting of the Institute in June.

Jacinto Steinhardt, formerly a physical chemist, National Bureau of Standards, has been awarded the President's Certificate of Merit by the Navy Department for "outstanding fidelity and meritorious conduct in aid of the war effort."

Dr. Steinhardt was cited for services as a member of the Anti-Submarine Welfare Operations Research Group, a a group of scientists under OSRD, in devising original and effective tactics for aircraft in combating submarines and intercepting enemy blockade. He is now director of research of the successor organization, the Operations Evaluation Group, scientists and mathematicians engaged in scientific analysis of naval tactics, strategy, and new developments, furnished to the Office of the Chief of Naval Operations by Massachusetts Institute of Technology.

The Department of Obstetrics and Gynecology, University of Utah School of Medicine, was recently awarded the 1946 prize for outstanding clinical investigative work, presented by the Central Association of Obstetricians and Gynecologists. The work was described in a paper, "Menorrhagia Associated With Irregular Shedding of the Endometrium," presented by the authors, E. G. Holmstrom and C. E. McLennan, at a meeting of the Association in Chicago.

J. C. Geiger, director of public health, city and county of San Francisco, California, has been granted the Grand Ducal Order of the Oak Crown, House of Nassau, Grand Duchy of Luxembourg, founded as an Order of Merit in 1841. Dr. Geiger received the decoration through the foreign minister "for distinguished service to the Duchy of Luxembourg and its citizens and as a great humanitarian in the field of public health."

The Morris Liebmann Memorial Prize of the Institute of Radio Engineers has been awarded to Albert Rose, Radio Corporation of America Laboratories, Princeton, for 1946, and to J. R. Pierce, Bell Telephone Laboratories, New York, for 1947. Formal presentation was made at the Institute's annual dinner, Hotel Commodore, New York, March 5.

Dr. Rose, who has specialized in research in the field of television camera tubes, received the prize for work on the image orthicon picture tube, and Mr. Pierce, who has worked on high-frequency tubes, for his part in developing the traveling-wave type of tube.

Jerome P. Webster, Columbia-Presbyterian Medical Center, New York, was recently made a Commander of the Greek Order of the Phoenix for his work in restoring the features and limbs of Greek Army fliers wounded in the war. Presentation was made by John D. Kalergis, Greek Consul General, in New York.

E. Newton Harvey, Henry Fairfield Osborn professor of biology, Princeton University, has been awarded the grade of officer of the "Ordem Nacional do Cruzeiro do Sul" by the Brazilian Government, in appreciation of a series of lectures on biophysics delivered at the Instituto Biofisica in April 1946.

The Jane Coffin Childs Memorial Fund for Medical Research made the following appropriations on November 15, 1946, and February 21, 1947, a total of $202,616.66 in support of cancer research projects and fellowships:

F. Duran-Reynals, associate professor of bacteriology, Yale University School of Medicine, $49,500 for 3 years, 1947–50, for continued study of viruses and cancer.

J. Engelbreth-Holm, professor of pathology, University of Copenhagen, Denmark, $3,000, 1947, 1948, for continued study of the factors influencing carcinogenesis by chemicals.

W. U. Gardner, professor of anatomy, Yale University School of Medicine, $16,500, 1947–50, for continued investigations of the role of hormones in normal and abnormal growth.

Alexander Haddow, director, and his associates at the Chester Beatty Research Institute of the Royal Cancer Hospital (Free), London, England, $5,000, 1947–48, for continued support of the Institute's research program on chemical carcinogenesis, viruses and cancer, and chemotherapy of cancer.

J. G. Kidd, professor of pathology, Cornell University Medical College, $14,580, 1947–50, for continued study of viruses and cancer.

C. C. Little, director, and P. A. Gorer, guest investigator, Roscoe B. Jackson Memorial Laboratory, supplement of $1,000, 1946–47, to assist in Dr. Gorer's collaboration on investigations of immunological aspects of genetics.

C. P. Rhoads, director, and his associates at Memorial Hospital and Sloan-Kettering Institute for Cancer Research, $10,000, 1946–47, for continued chemical and metabolic studies of cancer with special reference to steroids.

W. T. Salter, professor of pharmacology, Yale University School of Medicine, $546.66 for 6 months, 1946, for biochemical studies of enzymes and steroids in relation to malignancy.

L. C. Strong, associate professor of anatomy, Yale University School of Medicine, $41,290, 1947–50, for continued genetical investigations of cancer.

J. C. Turner, assistant professor of medicine, Columbia University, College of Physicians and Surgeons, $8,000, 1947, 1948, for study of viruses and cancer.

Donner Foundation, for continued contr bution to support of the journal, *Cancer Research*, $5,500 for 1947.

Yale University School of Medicine, supplement of $500, 1946–47, for replacement of equipment in animal house.

C. G. Baker, fellow, $1,800, 1947–48, to work with D. M. Greenberg, Division of Biochemistry, University of California, Berkeley.

J. B. Goetsch, fellow, $3,000, 1947–48, to work with C. L. Deming, Section of Urology, Department of Surgery, Yale University School of Medicine.

D. A. Karnofsky, fellow, $13,500, 1946–49, to work with C. P. Rhoads at Memorial Hospital and the Sloan-Kettering Institute for Cancer Research.

Joshua Lederberg, fellow, $2,400, 1947–48, to work with E. L. Tatum, Department of Botany, Yale University.

B. L. Newton, reappointed fellow, $3,500, 1947–48, to work with H. S. N. Greene, Departments of Surgery and

Pathology, Yale University School of Medicine.

Stanfield Rogers. fellow, $3,500, 1947–48, to work with Peyton Rous, Rockefeller Institute for Medical Research.

W. C. Schneider, fellow, supplement of $500, 1946–47, while working with Albert Claude, Rockefeller Institute for Medical Research.

J. E. Sokal, fellow, $9,000, 1947–50, to work with C. N. H. Long and H. S. N. Greene, Departments of Physiological Chemistry and Pathology, Yale University School of Medicine.

An allocation of $10,000 for 1947–48, to be used for expenses of conferences, lectures, consultants, and travel of investigators receiving grants from the Fund. A commitment of $4,500 has been made from this allocation to help bring foreign investigators to the United States for the Fourth International Cancer Research Congress in St. Louis, September 1947. A commitment of $3,000 has been made from a similar allocation for 1946–47 for the organizing and operating expenses of the Congress.

Colleges and Universities

The Harvard School of Public Health announces that Thomas M. Rivers, director of the Hospital of the Rockefeller Institute for Medical Research, will deliver the Cutter Lecture on Preventive Medicine in Amphitheatre D of the Harvard Medical School on April 22 at 5:00 P.M. Dr. Rivers' subject will be: "Certain Public Health Aspects of Infectious Diseases."

The Tulane University Council on Research has provided $12,350 for a five-year study of the reptiles and amphibians of Louisiana. The program, under Fred R. Cagle, associate professor of zoology, is designed to define species and accumulate data on reptile populations and histories. An expedition to western Louisiana and eastern Texas is planned for the summer of 1947.

Long Island University, Brooklyn, New York, has announced promotion of Curtis L. Weathers to professor and chairman of the Department of Biology, and Harold M. Messer to associate professor of biology.

The University of Hawaii opened its 40th anniversary celebration with a traditional island feast March 15. The following three college presidents were among U. S. speakers at the celebration: Karl T. Compton, Massachusetts Institute of Technology; Howard L. Bevis, Ohio State University; and Charles Seymour, Yale University. Gregg M. Sinclair, president of the University of Hawaii, extended invitations to these and other U S. participants.

Stanford University has announced the following appointments to begin in September 1947: Charles E. McLennan, professor and head of the Department of Obstetrics and Gynecology, University of Utah School of Medicine, has been named to the same position at the Stanford School of Medicine, San Francisco; Leonard I. Schiff, University of Pennsylvania physicist who worked on the Los Alamos project, associate professor of physics; and Josephine R. Hilgard, director of the Child Guidance Clinic, Children's Hospital, San Francisco, associate clinical professor of medicine.

The Ohio State University announces promotion of Julian B. Rotter to associate professor psychology and Abraham Edelmann to instructor of physiology.

Meetings

The South Carolina Academy of Science will hold its annual meeting in Columbia, South Carolina, on April 26 together with the Junior Academy of Science.

Over 30 papers have been scheduled for the Senior Academy meeting. Papers will be presented by those competing for the Jefferson Award, offered by Phipps and Bird, of Richmond, Virginia, for a paper based on original research.

A symposium on "Recent Advances in the Investigation of Venereal Diseases," to be held in the auditorium of the Federal Security Building, Washington, D. C., beginning at 9:30 A.M. on April 17, has been announced by J. E. Moore, chairman of the Syphilis Study Section of the National Institute of Health. Although it is not possible for the Study Section to defray travel expenses, all interested persons are invited to attend. Copies of the program will be sent upon request. All inquiries should be addressed to Dr. Gordon Seger, Executive Assistant, Syphilis Study Section, National Institute of Health, Bethesda 14, Maryland.

The Federation of American Societies for Experimental Biology announces that hotel rooms are still available for its May 18–22 meeting in Chicago. Requests should be addressed to Dr. F. J. Mullin, University of Chicago College of Medicine, Chicago 37, Illinois.

The Society of American Foresters will hold its annual meeting in Minneapolis, December 18–20, 1947, with headquarters in the Hotel Nicolett. E. L. Demmon, director of the Lake States Forest Experiment Station, St. Paul, is chairman of the program committee.

Elections

At a meeting of the Branner Geological Society of Southern California, California Institute of Technology, Pasadena, March 5, Vernon L. King, consulting petroleum geologist, was made president; Richard Jahns, California Institute of Technology, vice-president; and William H. Easton, University of Southern California, secretary-treasurer.

Emil Witschi, professor of zoology and experimental biology, State University of Iowa, has been elected a corresponding member of the Swiss Society of Genetics.

Recent Deaths

H. Van Gent, 47, head of the Johannesburg Observatory, died March 31 in Amsterdam. Dr. Van Gent's collection of astronomical photographs formed the basis for important investigations of the central structure of the Milky Way.

W. B. Scott, 89, professor emeritus of geology and paleontology at Princeton University, died March 29 in Princeton. Winner of the Wollaston medal of the Geological Society of London in 1910, Dr. Scott was an internationally known authority on fossil mammals.

R. S. Greene, 65, former general director of the China Medical Board of the

Rockefeller Foundation and vice-director of Peiping Union Medical College since 1929, died March 27 in West Palm Beach.

Juan Noé, 70, director of the Instituto de Biología of the Universidad de Chile, died January 22 in Santiago. In addition to serving on the faculty of the University for 35 years, Dr. Noé was instrumental in the sanitation of large malaria areas in northern Chile and was in large part responsible for the founding of the Institute.

A letter has been received from Abdul Majid, president of the University of Kabul, Afghanistan, asking support of American bacteriologists in rebuilding the reprint collection of his university. Sanford Elberg, Department of Bacteriology, University of California, Berkeley, who received the letter, said the Afghanistan institution has received nothing in bacteriological literature since 1940 and is especially in need of material on microbiology and public health.

The Committee for the Study of Animal Societies Under Natural Conditions held its first meeting in New York, January 31 and February 1, under auspices of the New York Zoological Society, following arrangements made at the Conference on Genetics and Social Behavior, Roscoe B. Jackson Memorial Laboratory, last summer.

At the New York meeting J. P. Scott was elected executive secretary to coordinate activities of the Committee. The following were made chairmen of subcommittees on special research projects: C. R. Carpenter, Jackson Hole Research Project; T. C. Schneirla, subcommittee to survey locations and institutions in which research on animal social behavior and organization is possible; and Fairfield Osborn, ways and means.

Purpose of the conference was to help organize a research program on animal behavior, particularly in connection with the New York Zoological Society's new station at Jackson Hole, Wyoming. Action was also taken on the Barro Colorado Island Biological Station, which, the Committee believes, needs to be put on a permanent basis of support as a center of tropical research.

The secretary's office, it is hoped, will be a clearinghouse for research ideas and projects of various individuals and institutions. Correspondence should be addressed to J. P. Scott, Roscoe B. Jackson Memorial Laboratory, Bar Harbor, Maine.

Research on the fundamental principles of phosphate fixation and release by soils, utilizing radioactive phosphorus, will be conducted by the North Carolina Agricultural Experiment Station, Raleigh, under a grant from the Phosphate Research Committee of the fertilizer industry. The Experiment Station has arranged for cooperation with the New York Agricultural Experiment Station, Ithaca, and Bureau of Plant Industry, Soils, and Agricultural Engineering, USDA, Beltsville, Maryland.

The technical committee, representing industry, consists of H. B. Siems, Swift & Company; R. R. Hull, I. P. Thomas and Sons Company; H. E. Hendricks, Knoxville Fertilizer Company; F. E. Boyd, Virginia Carolina Chemical Corporation; and V. Sauchelli, Davison Chemical Corporation, chairman.

The American Society of Professional Biologists has intensified its organizational activities due to response to the article, "A Society for All Biologists," which appeared in *Science*, October 4, 1946. Copies of the proposed constitution and applications for membership may be obtained from Roy F. Fritz, 605 Volunteer Building, Atlanta, Georgia, or Norman C. Laffer, Department of Bacteriology, University of Maryland, College Park, Maryland.

A Swedish zoological expedition of six members, headed by Åke Holm and Bergt Lundholm, Upsala University, will investigate the fauna on Kilimandjaro and a number of other East African peaks, on which various animal species from earlier and more humid epochs have survived. The expedition is expected to leave Sweden in the fall and spend about a year in Africa.

The first natural history museum in Iraq was established in Baghdad early in 1946 and is now operating under the auspices of the Iraq Ministry of Education.

According to Bashir E. Allouse, director, and member of the AAAS, the Iraq Natural History Museum consists of three main sections: Zoological Section, with exhibits of the avifauna of Iraq and small collections of Iraq mammals, reptiles, fishes, and invertebrates; Botanical Section, with plaster-made models of Iraqi fruits and vegetables and specimens of plant products, economic plants, and plant diseases; and Geological Section, with a cement model of the geological structure of Kirkuk oil fields, presented by Iraq Petroleum Company, and a model of an oil refinery, oil products, and other items, presented by the Rafidain Oil Company, as well as specimens of rocks, crude oil, and fossils found in Iraq.

The museum seeks contacts with similar museums in the U. S. and other countries with a view to exchanging information and publications. Contributions of books, periodicals, and bulletins should be sent to the Director, Iraq Natural History Museum, Baghdad, Iraq.

An International Trust for Zoological Nomenclature has been established for the purpose of managing the financial, commercial, and other business affairs of the International Commission on Zoological Nomenclature, according to Francis Hemming, secretary of the International Commission, who writes:

"In view of rapid growth in recent years in the volume of its work, the International Commission on Zoological Nomenclature, an unincorporated body of 18 international commissioners elected by the International Zoological Congress, recently formed an incorporated body under United Kingdom law with the title, International Trust for Zoological Nomenclature. At the same time the International Commission has transferred its assets to the International Trust and the Trust has accepted responsibility for all liabilities of the Commission.

"Under the new arrangements, the Commission will continue all its scientific functions while the Trust will be responsible for publishing the Commission's *Opinions* and other publications, meeting its administrative expenses, and carrying out such further developments as may be decided on by the Commission.

"Members of the Commission will be members of the Trust and the secretary to the Commission will be secretary *ex-officio* to the Trust. The Trust has taken over as its registered office 41, Queens Gate, London, S.W.7., hitherto occupied by the Commission. The Commission has

arranged for appointment of certain honorary unpaid officials of the Commission as members of the Trust to ensure that there will at all times be a sufficient number of members available to attend meetings of the Trust. At invitation of the Commission chairmanship of the Trust has been accepted by Col. the Rt. Hon. Walter Elliot."

Full text of the instrument of incorporation will be published in an early issue of the Commission's *Bulletin of Zoological Nomenclature*.

The foundation stone was laid November 21, 1946, for an $11,000,000 National Metallurgical Laboratory at Jamshedpur, India, part of a program of the Indian Council of Scientific and Industrial Research and the Government of India to establish a chain of 7 research laboratories in different parts of the country.

According to G. P. Contractor, Research Laboratories, The Tata Iron & Steel Company, Ltd., Jamshedpur, the laboratory will cover both fundamental and applied metallurgical research. A descriptive note from Dr. Contractor states: "Provision has been made in final plans of the National Metallurgical Laboratory for administration, including statistics, library, museum; chemical analysis, physical chemistry, physics as it affects metallurgical problems; examination, preparation, and smelting of metallic ores; melting, heat treatment, and working of metals and alloys; research into the structure and physical properties of metals and alloys; electrodeposition and surface treatment of metals; and research on refractories."

The laboratory will consist of a main building and separate technological block. The main building, containing offices, laboratory, museum, theater, and library, will have three floors with a total of 60,600 square feet of working area. The technological block, with large workshop laboratories and associated control rooms, will provide working floor area of about 28,000 square feet.

Early in January cornerstones were laid for the new National Physics Laboratory, modeled on our National Bureau of Standards, and for a Laboratory of Industrial Research, both in Delhi. The Central Glass and Ceramic Research Institute in Calcutta and the Fuel Research Institute, Dhanbad, in addition to the National Metallurgical Laboratory, were founded during 1946.

Harlow Shapley, director, Harvard College Observatory, and president, AAAS, who was a guest of the All-India Science Congress in Delhi during January, observed Pandit Jawaharlal Nehru, leader of the Congress Party, accept presidency to the newly-created Association of Scientific Workers of India, to be assembled from the faculties of the 20 universities in India and from the technical workers in the textile, steel, jute, and other factories.

The food research and development program of the Quartermaster Corps, Chicago, has expanded 50 per cent since V-J Day and now has a staff of 250, occupies 120,000 square feet of floor space, has an equipment inventory of $500,000, and an annual operating budget of approximately $2,000,000.

The Institute is a coordinating center, working with more than 500 industrial laboratories on food, ration, and container development problems, and with more than 80 colleges, universities, and other research institutions on fundamental problems in food research. Results of this effort are more than 300 food and ration specifications, basis of the food procurement program for the armed forces. From a technological standpoint, the Institute is operated almost entirely by civilian scientists and technologists.

According to a letter received from Guido Grandi, director of the Instituto di Entomologia della Università, Bologna, the Institute was destroyed by the Anglo-American bombardment, but by repeated removals during three years, partly preceding and partly following the bombardment, all of the library, collections, and apparatus were saved. The letter, received by J. C. Bradley, professor of entomology, New York State College of Agriculture, Cornell University, states that the Institute is now in reconstruction and has fully resumed its activities. Publication of the *Bolletino* has been continued, and the 15th volume will shortly be issued.

The Societa Entomologica Italiana was seriously and irreparably damaged, according to the letter, the bombardment having destroyed 50,000 volumes, though the *Bolletino* and *Memorie* are being continued in reduced scale.

Hui-Ling Li, professor of botany, Soochow University, and former member of the AAAS, is attempting to rebuild his botanical library following return to China in 1946, after six years work in this country. He would appreciate receiving reprints of papers from American botanists. They may be addressed to: Dr. Hui-Ling Li, Department of Biology, Soochow University, Soochow, China.

The National Registry of Rare Chemicals, Armour Research Foundation, 35 West 33rd Street, Chicago 16, Illinois, has submitted the following list of wanted chemicals: 1,18-octadecandioic acid; nucleoproteins; millite; gahnite; celsian; prismatin; sapphiran; tetrophan; 4 - amino - 2,2′ - dichlorobenzophenone; 4 - amino - 2,4′ - dichlorobenzophenone; eicosenol-1; talomucic acid; agaric acid; d-fucose; elaidic acid; pyrroline; tropic acid; d-quercitol; glucurone; and hydrindene.

The 20th Josiah Willard Gibbs Lecture was delivered by Subrahmanyan Chandrasekhar, of the Yerkes Observatory, University of Chicago, before the 53rd annual meeting of the American Mathematical Society, Swarthmore College, Swarthmore, Pennsylvania, in December. Dr. Chandrasekhar's subject was "The Transfer of Radiation in Stellar Atmospheres." By invitation, addresses were also given by A. P. Morse, University of California, on "Derivatives and Their Integrals," and Harald Cramér, University of Stockholm, on "Some Aspects of the Theory of Stochastic Processes." Seventy research papers were presented at the meeting, attended by over 500 people.

Make Plans for—

American Chemical Society, spring meeting, April 14–18, Atlantic City, New Jersey.

Association of Southeastern Biologists, 8th annual meeting, April 18–19, Emory University, Georgia.

Southeastern Section, Botanical Society of America, Inc., 4th annual meeting, April 18–19, Emory University, Georgia.

Institute of Mathematical Statistics, meeting on stochastic processes and noise, April 24–25, New York City.

American Geophysical Union, 28th annual meeting, April 28–30, National Museum, Washington, D. C.

COMMENTS

by Readers

Please! New York's city colleges have had a difficult enough time telling the American public of the good work they have done these many years. Your note on page 159 of the February 7 issue of *Science* on the death of Morris Raphael Cohen, identifying him as "professor of philosophy at the University of Chicago until his retirement in 1941," robs the City College of the most sparkling jewel in its diadem of scholars. It is true that Prof. Cohen taught one or two quarters at Chicago, but before that and for much of his productive life as mathematician, philosopher, writer, scholar, and teacher, from about 1912 to his retirement, he was a member of the Department of Philosophy, City College of New York.

In all the four New York city colleges, we were proud for many, many years to count ourselves as colleagues of Prof. Cohen, and it comes as something of a shock to us to find him identified simply with the institution at which he temporarily taught for a short interval after his retirement from the City College. (AUSTIN B. WOOD, *Brooklyn College, Brooklyn, New York.*)

Our interest in the fauna of Joshua Tree National Monument, on the Southern California desert, has taken A. J. Van Rossem and myself to the area on three occasions during the past winter (1946–47). The monument is confined to the "high desert" terrain of San Bernardino and Riverside Counties, the stations which we occupied ranging from 3,500 to 4,700 feet above sea level. Furthermore, this winter seems to have been slightly below average in temperatures. Observations were made during the first weeks of November, of December, and of February.

Daytime temperatures in direct sunlight were cool enough to make it uncomfortable to remain inactive without warm clothing. As soon as the sun dropped behind the San Gorgonio Mountain mass to the west, the air rapidly became cold. At 7:00 P.M. the temperatures would fall to 33°–38° F. At sunrise the temperatures would range between 20° and 28°. In short, the temperatures were winter temperatures for the area, and night temperatures remained low throughout the whole period of darkness.

During each visit to the monument, bats were seen or heard in active flight in air strata from head height to distances 40–50 feet above the ground. Small Lepidoptera occasionally came into the light of our campfire, and desert mosquitoes visited our sleeping bags though ice formed in our drinking water.

Once at dawn the bats came close enough to my head to give the impression of a small species—probably a *Pipistrellus*. On one occasion at 11:15 A.M. in bright, clear sunshine, a small, gray-brown bat with dark membranes came to the cattle trough at Quail Spring and dipped the surface of the water after the fashion of drinking swallows. The temperature four hours earlier had stood at 20° F.

The following conclusions seem justified: (1) The bats seen or heard were not in transit; (2) they remained active during a considerable portion of the night; (3) such activity could hardly be that of a hibernating animal temporarily aroused by warm periods of weather; (4) some insect food species are active at surprisingly low temperatures; (5) some species of bats have temperature tolerance of fairly wide range. (LOYE MILLER, *University of California at Los Angeles.*)

Some time ago the undersigned published a note, in the Dutch language, on the action of neutrons on hafnium, no other way of publication being available at the time (*Ned. Tijdschr. Nat.*, 1943, **10**, 258). As this paper is hardly accessible, it seems worth while to mention its contents here. With slow neutrons a period of 20 seconds was reported; with fast neutrons periods of 20 seconds, 10 minutes, and about 6 hours. As the stable hafnium isotopes are 174, 176, 177, 178, 179, and 180, the second period was supposed to be due to Hf^{175}, and it was recommended for the estimation of hafnium in mixtures with zirconium. It was also shown that zirconium could be determined in mixtures with hafnium by prolonged irradiation with fast neutrons. Under these circumstances no periods of the order of days were found in hafnium; after two days decay the activity of our hafnium sample amounted to only 2 per cent of that of a similarly treated zirconium sample.

Recently, A. Flammersfeld (*Z. Naturforsch.*, 1946, **1**, 190) also has observed the formation of a hafnium isotope with slow neutrons. Since he used (D + D) neutrons instead of (Li + D) neutrons, as we did, he has not been able to observe the formation by the (n; 2n) process. He was, however, able to carry out some absorption measurements of the radiation, which lead to the assumption that the 20-second isotope is an isomer, decaying with internal conversion. Of the mass numbers suggested by his experiments (175, 177, 178, 179, 180, and 181), this author rules out the first and the last by means of intensity considerations and the numbers 178 and 180 on the strength of a rule of Mattauch. Mass numbers 180 and 181 are definitely excluded by the activation with fast neutrons. (A. H. W. ATEN, JR., *Natuurkundig Laboratorium der N. V. Philips' Gloeilampenfabrieken, Eindhoven, Holland.*)

A new laboratory plant for the study of carbohydrate metabolism is recommended by John S. Bailey and Emmett Bennett, of Massachusetts Agricultural Experiment Station, Amherst, Massachusetts. The plant, *Impatiens Sultanii*, is a commonly used household ornament growing to the height of 12–24 inches. Exudates proved to be principally sucrose. The stems on a dry weight basis yield approximately 33 per cent reducing sugars as dextrose. Nonreducing sugars are present only in traces. Although the amount of sugar is only one-third to one-half that found in sugar beets or sugar cane, it is high compared with most other plants.

TECHNICAL PAPERS

The Effect of Body Temperature on the Duration of Barbiturate Anesthesia in Mice

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Both toxicity and duration of action of many central nervous system depressants are influenced by temperature. Most investigators have dealt chiefly with the influence of environmental temperature on the toxicity of these drugs (*4*). The few available investigations which have considered the influence of temperature on the duration of action have failed to specify the changes in body temperature resulting from exposure of the animals to varied environmental temperatures. The body temperatures of small animals at extremes of environmental temperature are well known to be unstable even without anesthesia. It is apparent that for the anesthetized animal the determination of environmental temperature alone is inadequate.

Cameron (*2*) and Gaylord and Hodge (*5*), using pentobarbital in rats, and Raventos (*7*), using evipal in mice, found the duration of sleep with a given dose of the barbiturate to increase with decrease in environmental temperature. Although body temperatures were not reported, it seems certain that marked changes must have occurred at the environmental temperatures employed.

In order to determine the influence of body temperature on the duration of action of some barbituric acid derivatives, the experiments summarized in Table 1 were carried out. Albino mice of both sexes were used, and the experiments with a given drug were performed simultaneously at two temperatures. To obviate differences in rate of absorption due to temperature, the animals were all injected at room temperature, which was maintained until anesthetization. Half of the group were then transferred to a chamber maintained at 35–37° C., and the other half were rapidly cooled to a body temperature of 25–27° C. by contact with a metal plate at approximately 0° C. The two groups were then maintained at *body* temperatures of about 37° C. and 27° C., respectively, by varying the rate of heat loss through warming or cooling. Body temperatures were determined in each mouse in rotation, using two potentiometers and iron-constantan thermocouples inserted rectally to a depth of 15 mm. Sleeping time was taken as the interval between loss and recovery of the righting reflex.

Table 1 shows that the duration of action of pentobarbital and Sandoptal[1] is greatly prolonged by a reduction in body temperature of 10° C., while that of barbital is scarcely affected by such a reduction in temperature. The chief difference between barbital and the other two derivatives studied lies in their fate in the body. Barbital (diethylbarbituric acid) is relatively stable and is readily excreted in the urine; its action is prolonged by bilateral nephrectomy but not by hepatic damage or by subtotal hepatectomy. Pentobarbital (ethyl-1-methylbutyl-barbituric acid) and Sandoptal (allyl isobutyl barbituric acid), on the other hand, are excreted in the urine only in traces; their anesthetic action is prolonged by liver damage or by hepatectomy but not by bilateral nephrectomy. Therefore, barbital is detoxified chiefly by urinary excretion, while pentobarbital and Sandoptal are detoxified by inactivation in the tissues, of which the liver probably is the most important. Sandoptal was included here because it is intermediate in duration of action but is readily inactivated by the tissues. Although the mechanism of tissue inactivation of pentobarbital, Sandoptal, and other short-acting barbiturates is not understood, it seems probable that it is enzymic in nature and that, in common with other enzymic processes, it is slowed by a reduction in temperature. Masson and Beland (*6*) have classified the barbiturates on the basis of the mechanism of detoxification (tissue inactivation or elimination by the kidney, or both). In general it is to be expected that the duration of action of those barbiturates which are inactivated in the tissues will be prolonged by a reduction in body temperature, while that of derivatives excreted by the kidney will be little affected by changes in body temperature, except for a possible

TABLE 1

DURATION OF BARBITURATE ANESTHESIA IN MICE AT TWO LEVELS OF BODY TEMPERATURE*

	Barbital	Pentobarbital	Sandoptal
Dose (Na salt) (mg./kg.)	290	37.5	55
Body temperature, 37°C.:			
No. of animals	12	11	9
Mean body weight (grams)	22.4	20.1	20.5
Mean sleeping time (min.)	314.5	17.6	76.9
Standard Error	20.02	3.33	12.21
Body temperature, 27°C.:			
No. of animals	11	11	7
Mean body weight (grams)	22.4	21.5	23.3
Mean sleeping time (min.)	331.5	61.8	202.7
Standard Error	22.14	4.51	20.08
P†	0.1	<0.001	<0.001
Ratio, $\frac{\text{Sleeping time, 27°C.}}{\text{Sleeping time, 37°C.}}$	1.05	3.5	2.6

* All barbiturates were administered intraperitoneally as the sodium salt in solutions of such strength that the dose was contained in 0.1–0.3 ml.

† P expresses the probability that the difference between the sleeping times at the two body temperatures would occur through errors in random sampling; see Fisher (*3*) for method of calculation.

[1] The Sandoptal was kindly supplied by Mr. Harry Althouse, Sandoz Chemical Works, West Coast Branch, San Francisco.

effect of this temperature on the rate of their excretion in the urine.

Many years ago Brunton (*1*) found that warming reduced the incidence of death in animals poisoned with chloral hydrate, a depressant which is largely detoxified by conjugation in the liver, and recommended that victims of acute chloral poisoning be kept warm. The data presented here also provide a rational basis for the application of warmth in cases of acute barbiturate poisoning involving short-acting barbiturates which are inactivated by the tissues.

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Hyperheparinemia: Cause of the Hemorrhagic Syndrome Associated With Total Body Exposure to Ionizing Radiation[1]

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Hemorrhage is one of the most striking features of the syndrome which follows acute whole-body exposure to ionizing radiations in the midlethal range. This irradiation-induced bleeding phenomenon occurs in man as well as in many experimental animals. In our experience the dog proved more suitable for study than the rabbit, guinea pig, rat, mouse, or goat, and the picture displayed by the dog later proved to be very similar to that seen in man following the bombing of Hiroshima and Nagasaki (*3*).

The hemorrhagic disease of irradiation is accompanied by a thrombocytopenia. Both bleeding and clotting times are prolonged, and clot retraction is impaired. At death, both animal and man show extensive hemorrhages which may occur in all organs of the body but which are first seen in the organs of motions, such as the intestines, heart, lungs, skeletal musculature, and urinary bladder.

This disease has been thought to result from the associated thrombocytopenia (*2*). However, in a study carried out on dogs during the past three years we have concluded that the thrombocytopenia plays only a secondary role in producing hemorrhage (*1*). Of greatest significance in this disease is the presence in the blood of an increased amount of free heparin. These conclusions are based on the following observations:

(1) The clotting time in both man and dog may be greatly prolonged or the blood rendered entirely incoagulable after acute exposure to ionizing radiations such as X-rays delivered over the entire body. If the clotting time is sufficiently prolonged, the blood of an irradiated dog will delay the clotting time of normal blood, thus demonstrating the presence of an active anticoagulant not normally present in blood.

(2) Evidence that this anticoagulant is heparin is based on the fact that specific antiheparin substances, such as toluidine blue and other members of the thionine series, and protamine

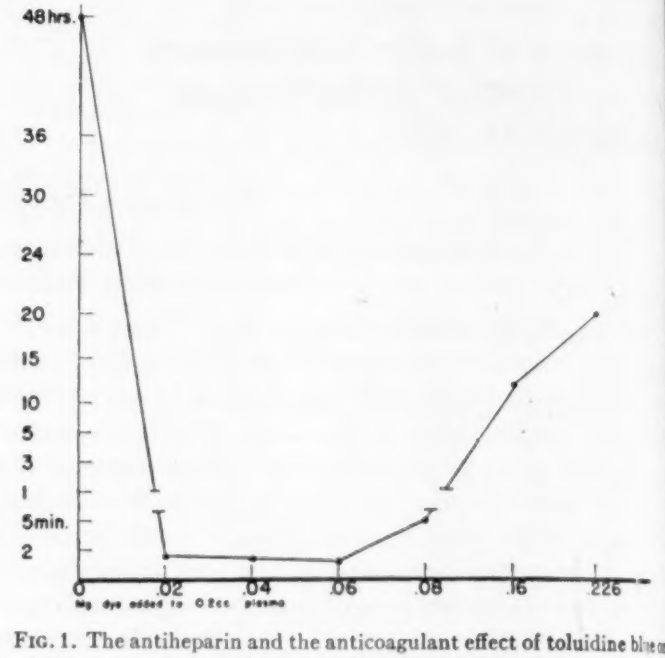

Fig. 1. The antiheparin and the anticoagulant effect of toluidine blue on the clotting time of plasma in an irradiated dog (Dog 108).

will return the clotting time to normal both *in vivo* and *in vitro*. These substances will prevent or stop hemorrhage even though the platelet count may be less than 50,000. The effect of toluidine blue on the *in vitro* clotting time of an irradiated dog is shown in Fig. 1. It will be noted that the dye is both coagulant and anticoagulant, and that its effective antiheparin range gives way to its anticoagulant property as the concentration of the dye increases. The clotting time of the blood of

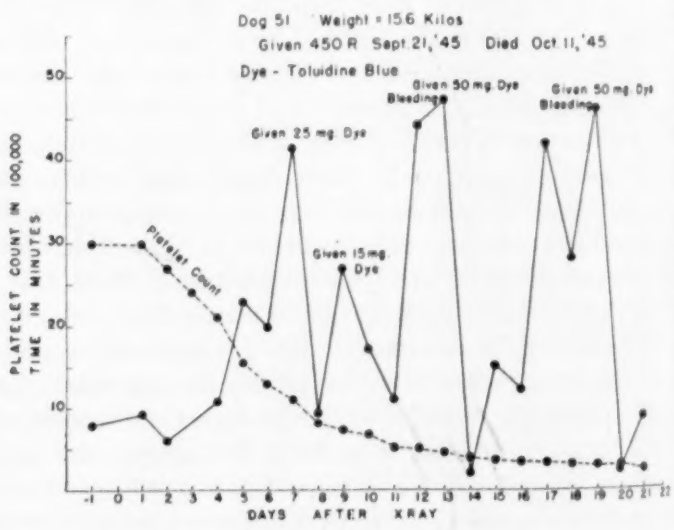
Dog 51 Weight = 15.6 Kilos
Given 450 R Sept 21,'45 Died Oct 11,'45
Dye - Toluidine Blue
Given 50 mg. Dye Bleeding
Given 50 mg. Dye Bleeding
Given 25 mg. Dye
Given 15mg Dye
Platelet Count
PLATELET COUNT IN 100,000
TIME IN MINUTES
50
40
30
20
10
-1 0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22
DAYS AFTER XRAY

Fig. 2. The effect of repeated injections of toluidine blue on the whole-blood clotting time of an irradiated dog.

this animal was greater than 48 hours, but after the intravenous injection of 24 mg. of toluidine blue the clotting time returned to normal within 20 minutes after dye administration.

(3) An anticoagulant which was indistinguishable from heparin, was isolated from the blood of irradiated dogs, and on the basis of the number of units of potency per milligram of

[1] This paper is based on work performed under Contract No. W-7401-eng-37 with the Manhattan Project for the University of Chicago. It will appear in Volume 22B of the *Manhattan Project Technical Series* as a part of the contribution from the University of Chicago Project.

weight the isolated material proved to be as active as our standard (Abbott) sodium acid salt of heparin. Our material was inactivated by both toluidine blue and protamine and was heat stable.

(4) Thrombocytopenia *per se* did not appear to play an important role in the development of hemorrhage because, while hemorrhage and thrombocytopenia always occurred in the same animal, the time of onset of each varied considerably and did not always coincide (Fig. 2). Moreover, when the dye was given, bleeding was controlled, but the platelet count, if reduced, was not raised.

(5) The administration of vitamin K, ascorbic acid, calcium salts, and fresh whole blood transfusions did not prevent the onset of hemorrhage or stop bleeding once it occurred.

These observations have led us to study the effect of toluidine blue on the course of the hemorrhagic manifestations associated with such diseases as ideopathic thrombocytopenia and acute leukemias. The preliminary results indicate that significant temporary alleviations of the hemorrhagic manifestations may be thus induced.

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Treatment of Plutonium Poisoning by Metal Displacement[1]

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The great increase in availability and use of radioactive elements since the advent of the chain-reacting pile has intensified the need for effective treatment of radioelement poisoning. Radium poisoning has been a recognized danger since 1925. At present we are concerned primarily with plutonium (Pu^{239}), which emits 140,000,000 alpha particles/mg./minute and has a half-life of about 24,000 years. Many of the long-lived radioelements, including plutonium, which find their way into the body are deposited mainly in the skeleton. An appreciable amount of plutonium is also found in the liver and spleen. The dangers of plutonium far exceed those of radium poisoning because of the relatively large quantities of plutonium available and because of the number of individuals exposed.

From a consideration of ion exchange principles it may be predicted that the excretion of plutonium from "plutonized" animals would be increased by treatment with large amounts of the soluble salts of certain metals. The metals considered were those possessing a high valence and a metabolism similar to plutonium, so that their concentration relative to plutonium in a given site could be preponderant. An ideal metal would combine maximum displacing properties with minimum toxicity. The treatment, called metal displacement therapy, utilizes an innocuous metal, zirconium, to hasten the removal of plutonium from the body. Although this is still in very early and preliminary experimental stages, the results obtained so far are encouraging.

TABLE 1

Effect of Zirconium and Sodium Citrate Treatment on the Urinary Excretion of Plutonium in Rats*

(Data expressed as average per cent of injected dose of plutonium excreted each day)

Days elapsed following Pu injection	Pu control	Treatment			
		Zirconium (100 mg. on 2nd hr. and 3rd day after Pu injection)	Zirconium (50 mg. on 2nd and 24th hr. after Pu injection)	Sodium citrate (4 ml. of 10% sol. on 2nd hr. and 3rd day after Pu injection)	Sodium citrate (2 ml. of 10% solution on 2nd and 24th hr. after Pu injection)
0–1	0.75	8.2	5.1	3.2	3.1
1–2	.051	.12	.66	.07	.68
2–3	.027	.032	.060	.037	.041
3–4	.041	.60	.078	.19	.041
4–5	.045	.022	.060	.016	.023
5–7	.022	.07	.058	.011	.018
7–10	.021	.064	.083	.020	.017
10–12	.024	.060	.059	.021	.010
12–14	.016	.064	.053	.026	.022
Total Pu excreted in urine for 14-day period.....	1.1	9.6	6.5	3.7	4.0

* The rats (200-gram females) received 1.1 mg. of Pu/kg.

From a series of preliminary experiments dealing with the excretion of plutonium by rats after intravenous injections of aqueous solutions of lanthanum, cerium, and zirconium salts, it was concluded that, of those tested, zirconium was the most promising metal on which to concentrate effort.

The injection solution used contained from 20 to 25 mg. of zirconium dissolved in 10 per cent sodium citrate.

Young adult (200 grams) albino female rats and a young mongrel dog were used. The time at which zirconium treatment was begun, following the intravenous injections of plutonium, varied from two hours to five months, in the case of the dog. The rats received intraperitoneal and the dog intravenous injections of the zirconium citrate solution.

The effect of zirconium treatment on the urinary excretion of plutonium is shown in Table 1. The administration of zirconium in those rats treated shortly after the injection of plutonium was followed by as much as a 15-fold increase in the amount of plutonium excreted in the urine over a 24-hour period. When the output of plutonium had dropped, a reinjection of zirconium was followed by a second rise in the elimination rate. Actually, the reinjected rats excreted nearly as much plutonium on the fourth day following plutonium administration as the control rats eliminated during the first 24 hours. Finally, the sustained therapeutic action was shown by the observation that the excretion

[1] This report is based on work begun early in 1945 and performed under Manhattan District Contract No. W-31-109-eng-38 at the Metallurgical Laboratory of the University of Chicago and the Argonne National Laboratory, Chicago.

[2] Present address: Department of Physiological Chemistry, Medical School, University of Minnesota, Minneapolis 14.

The writer wishes to express his appreciation for the cooperation and technical assistance of members of the Medical and Biology Divisions, Argonne National Laboratory.

level remained about three times greater than that of the controls for several days after the cessation of zirconium therapy.

A small part of the heightened excretion was due to the sodium citrate solvent. However, the amount of plutonium eliminated by the animals treated with sodium citrate alone fell abruptly to pretreatment levels after the sodium citrate injections were discontinued.

None of the treatments significantly altered the quantity of plutonium excreted in the feces.

Tissue analyses revealed that the zirconium-treated rats had only about half as much plutonium in the skeleton and in the liver as the control animals, but the concentration of plutonium in the muscle and kidneys of these animals was greater than that found in the controls. The bone and liver concentrations of plutonium in the rats treated with sodium citrate did not seem to differ appreciably from those in the controls.

Five months after the dog received an intravenous injection of 0.058 mg. of plutonium/kg. treatment with very small doses of zirconium citrate (4–16 mg./kg. of body weight), injected intravenously, was begun. A very definite increase in urinary excretion of plutonium occurred within the first few days following each dose of zirconium. The extent of the rise in the elimination rate in the urine was directly proportional to the amount of zirconium injected. The increased rate of excretion was continued for at least three weeks after the cessation of zirconium treatment. Even with these dosage levels, which were far below the maximal dose by a factor of at least 10, the elimination rate of urinary plutonium was increased more than 150 per cent over the pretreatment level.

The average excretion of plutonium in the feces of the dog, following the zirconium treatment, appeared to increase but slightly.

In rats treated with zirconium about five weeks after the injection of plutonium, a roughly 10-fold increase in the urinary excretion of plutonium was observed. These animals were sacrificed shortly after treatment and were found to have only half as much plutonium in the liver as the controls. The bone content of plutonium was unchanged.

It appears, therefore, that zirconium first acts to displace plutonium from the liver. Later it migrates to the bone and slowly but continuously displaces the deposited plutonium to an extent which depends on the concentration of zirconium relative to the plutonium.

Radioautograph studies (*1*) have shown that plutonium, cerium, yttrium, and zirconium are laid down in the uncalcified organic matrix of the bone and in the endosteum and periosteum. Strontium, on the other hand, is deposited almost exclusively in bone salt, and it might be expected that zirconium treatment would have little effect in cases of radiostrontium poisoning. This was shown experimentally where it was found that zirconium treatment had only a negligible effect on the excretion rate of radiostrontium and on its concentration in the liver and bone of rats. Experiments to test the effect of zirconium treatment in cases of radioyttrium poisoning are in progress.

A study of the toxicity of zirconium and other metals revealed that zirconium was by far the safest for therapeutic use. When zirconium was given in single massive doses of 1.5, 1.75, and 2.0 grams/kg. of body weight, the percentages surviving were 100, 50, and 0, respectively. No harmful chronic effects have as yet been found.

Within 24 hours after the injection of zirconium, 80–90 per cent of the metal was excreted in the urine. Its fecal excretion is, however, very low.

The action of sodium citrate in promoting the excretion of plutonium can be attributed to its ability to increase the diffusibility of plutonium (*2*) and thus facilitate its clearance through the kidney.

Further investigations of metal displacement therapy in cases of chronic poisoning by plutonium and other long-lived radioelements are in progress.

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Effect of Temperature on the Growth and Sterility of Maize

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Connecticut Agricultural Experiment Station, New Haven, Connecticut

Varieties of corn grown in the Northeast and in the Middlewest at the same latitude are noticeably taller in the East. Several environmental conditions, principally light intensity and temperature, are involved in this growth difference. Plants of many species, including maize, grown under tobacco shade cloth are significantly taller and broader in leaf than plants from the same lot of seed grown in full sunlight. Under the cloth shade the temperature is the same as outside, but the humidity is higher and the light intensity is lower. The same effect is noticed in the field, where short-stalked varieties of corn are grown in single rows between taller varieties. Where there is a wide alley between ranges, the plants at the ends of the rows are shorter than those in the center of the rows, the plants graduating in height. Here humidity and temperature are the same, but light intensity varies.

Some corn seedlings started in the greenhouse and set outdoors were shorter at maturity than plants from the same seed started outdoors. This indicated that temperature in the early stages of growth had an effect. To test this, seeds of a uniform, vigorous, first-generation hybrid ($WF_9 \times P8$) were germinated in an incubator at about 30° C. until the shoots and roots were from $\frac{1}{4}$ to $\frac{1}{2}$ inch long. Three different lots of these sprouted seedlings were held at 40, 50, and 60° C. for one hour, after which they were planted in pots and left in the greenhouse until it was certain the plants would grow. They were then set in the field alongside plants from the same lot of seed sown in the open ground at the same time the treated seedlings were started in the incubator. Some of the heat-treated seedlings died, but enough were started in each lot and later thinned to give an even stand of plants in the field.

All three lots of heat-treated seedlings were shorter in height, less vigorous in growth throughout the season, and later in flowering than the untreated plants. All lots grew to full maturity and were measured after growth had ceased. The results in inches of height were: control, 101; 40° C., 87; 50° C., 89; and 60° C., 93, *i.e.* an average of 90 inches in

height for the heat-treated lots compared to 101 inches for the control.

An unanticipated result was the pollen sterility in all treated lots. Normal tassels were produced with well-developed florets, but the anthers were small and shriveled and for the most part remained enclosed in the glumes. In view of the fact that high temperatures sterilize the male germ cells in animals from amphibians to mammals, these results are highly significant. This influence on growth is an antivernalization effect and may have wide usefulness in the production of hybrid seed, especially if it is shown by plants other than maize. Further experiments are in progress.

Failure of Sodium Salicylate to Inhibit Hyaluronidase *in Vitro*

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When India ink or Evans Blue was injected with hyaluronidase into the skin of rabbits or human subjects following the administration of sodium salicylate, Guerra (*1*) observed decreased spreading as compared with normal controls. If this result was due to the inhibition of hyaluronidase by sodium salicylate, as concluded by Guerra, it should be possible to demonstrate an antagonistic effect of sodium salicylate on hyaluronidase *in vitro*.

Using the broth culture filtrate of a mucoid group A streptococcus as substrate, it was found that 0.005 ml. of a crude bovine testicular extract completely destroyed 0.5 mg. of hyaluronic acid. The addition to the reacting mixture of 5 mg. of sodium salicylate did not decrease the rate of disappearance of the hyaluronic acid, the amount of which was estimated by precipitation with acidified dilute horse serum (*3*).

In a second experiment, 1:100 dilution of crude testicular extract was prepared in 10 per cent sodium salicylate. This solution, as well as a 1:100 dilution of the same testicular extract without sodium salicylate, was tested for its ability to prevent the mucin clot formation by potassium hyaluronate prepared from human umbilical cord (*2*). Both solutions prevented clot formation, again indicating no inhibition of testicular hyaluronidase by the sodium salicylate.

The action of sodium salicylate on streptococcal hyaluronidase was also examined. A broth culture filtrate of a nonmucoid group A streptococcus as a source of the enzyme was combined with a filtrate of a mucoid group A streptococcus containing hyaluronic acid. The enzyme destroyed 0.5 mg. of hyaluronic acid on incubation overnight. The inclusion of 0.1 per cent sodium salicylate in the system did not alter the reaction. When broth containing 10 mg. per cent of hyaluronic acid was inoculated with a nonmucoid group A streptococcus, the hyaluronic acid was destroyed by the time maximum growth was attained. The addition of sodium salicylate to the broth did not retard the disappearance of the hyaluronic acid except in concentrations that inhibited growth. Sodium salicylate, 0.1 per cent, was slightly bacteriostatic; 0.05 per cent inhibited neither growth nor the destruction of the hyaluronic acid.

These experiments fail to demonstrate any inhibitory effect of sodium salicylate on testicular or streptococcal hyaluronidase.

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The Carcinogenic Action of Smegma[1]

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Carcinoma of penis does not occur in people who have been circumcised in the first weeks of life and is rare in people who have been circumcised in childhood or in early puberty. Circumcision in adult life does not affect the frequency of the disease. Phimosis seems to be a predisposing factor. Penile cancer is frequent where personal hygiene is poor; it is rarer where bathrooms are plentiful. All this has been known for decades, and various opinions have been expressed concerning causal relations. Little has been done, however, to establish experimentally the possible carcinogenic action of smegma. Fishman, Shear, Friedman, and Stewart (*1*) injected filtered suspensions of human smegma subcutaneously into 12 young mice of the A strain. No tumors were obtained either in these mice or in 20 young mice into whose distended vaginas smegma was introduced.

In our experiments mice of the Paris R 3 strain were used. No spontaneous malignant tumors of skin and no cutaneous papillomata have been observed in many thousands of mice of this strain in the Crocker Cancer Research Institute. Some of the mice were bred in the Crocker Institute, others in Beth Israel Hospital. They were kept in wooden cages with wire covers, were fed Rockland pellets, and were given water.

Since human smegma, which was used in the first experiments, could not be obtained in sufficient amounts, horse smegma was substituted. This particular substitution was made because penile cancer is frequent in the horse. Smegma is best obtained from dead horses in rendering plants or from anesthesized animals in a department of veterinary surgery. The smegma was kept dry in glass jars in the refrigerator or at room temperature. Generally it was impossible to discover whether the material came from a stallion or from a gelding. One batch was examined for male and female sex hormones, but none were found.

The nonsaponifiable fraction was prepared in the usual way. An analysis for fatty substances gave the following result: total fat, 45 per cent of dry substance (fatty acids, 32.2 per cent; phosphatids, 3.9 per cent; total cholesterol, 6 per cent; cholesterol esters, 2 per cent).

Cerumen, which resembles smegma in being a skin product that is retained on or near the surface of the body, was used

[1] This study was aided by a grant from the Dora Paul Cancer Research Fund.

as control substance. This could be used because carcinoma of the auditory meatus is very rare in man and animals.

Method

A buried skin tunnel, as described in a previous publication (*2*), was made in midline in the middorsal region. Its walls consisted of skin and panniculus carnosus. The smegma, or the cerumen, was kneaded with water into a pulp thin enough to pass through the nozzle of a 2-cc. syringe (bore admitting catgut #3). No needle was used. The nozzle of the syringe was pushed gently into the caudad opening of the tunnel, and the plunger was pushed slowly until the material appeared at the cephalad end. When the skin tunnel broke down (which happened in about 40 per cent of the operations), the substances were injected under the skin or, in the case of the nonsaponifiable fraction, painted on the shaved skin. Benzol was painted on the skin or in the tunnel of 26 control mice. The injections were given every three weeks and sometimes every two weeks. The nonsaponifiable fraction was applied every week or alternated weekly with benzol, in an effort to check the regrowth of hair.

Of the 800 mice used, 250 died too early. Four hundred were treated with smegma. In 190, smegma was put into the skin tunnel; 122 received subcutaneous injections of smegma; and in 88, the suspension of the nonsaponifiable fraction was painted into the tunnel or on the skin surface. Most of the 150 mice which served as controls were treated with cerumen. The mice were operated upon when one month old. The average age at which treatment was started was 65 days for the smegma-treated mice and 68 days for the controls.

Results

There was no significant difference in the survival rates of treated and control mice up to the 400th day of life: 85 and 88 per cent, respectively, after 200 days; 74 and 80 per cent after 300 days; 65 and 57 per cent after 400 days. After 500 days, 47 per cent of those treated with smegma were alive as compared with 30 per cent of the controls. From the 600th day on, there was a marked difference (26 and 6 per cent, respectively), and, on the 700th day, the survival rates were 12 and 1½ per cent. The survival rate of the mice treated with the nonsaponifiable fraction was higher than that of the mice treated with whole smegma.

Microscopic sections of skin and inner organs were available for 212 of the 400 mice treated with smegma and for 80 of the 150 controls. Lung adenomas were found 15 times in the sections of the treated mice and twice in the controls. For lymphoid tumors and leukemia the figures were 15 and 5. Mammary carcinoma occurred 21 times in 105 treated female mice and 3 times in 40 female controls. The mammary tumors did not appear at an earlier age than is usual in the Paris strain. There were eight other spontaneous tumors, six appearing in the mice treated with smegma (adenocarcinoma of kidney, anal papilloma, two so-called hepatomas, one less differentiated carcinoma of liver, one inguinal rhabdomyosarcoma) and two in the controls (hepatoma, perianal subcutaneous spindle-cell sarcoma).

No tumor was found at the site of treatment in any control mouse. The one subcutaneous spindle-cell sarcoma found was situated far away from the site of treatment. *Tumors occurring in smegma-treated mice at the site of treatment included:* four papillary warts, two hornifying squamous-cell carcinomas (one with metastases), one undifferentiated skin carcinoma, and one spindle-cell sarcoma with metastases. Three of the papillary warts were cytologically regular; the fourth, in places, was carcinoma-like. The intrathoracic metastases of one carcinoma contained horn pearls.

There was much variation in the time interval between the starting of treatment and the first evidence of tumor: 36, 82, 122, and 247 days for the warts; 130 days for the sarcoma; 220 and 423 days for the carcinomas. (In the case of one carcinoma the figure is not available.) Thirty-six days is a short but not impossible interval.

The percentage of positive cases was about the same, whether whole smegma (6 in 190) or the nonsaponifiable fraction (3 in 88) was used. Of the four warts obtained, three followed the smegma treatment; of the four truly malignant tumors, two arose after use of whole smegma and two after the nonsaponifiable fraction. No tumors developed at the site of subcutaneous injection of smegma in 122 mice.

Discussion

Considering the nature of the substance used, no strong carcinogenic action (high percentage of positive results) was expected. That any tumors resulted from treating a skin surface with a product of skin epithelium or skin glands might be surprising. At the site of application of a similar substance (cerumen) in 150 mice, no tumors were found.

Among other differences between the smegma-treated mice and the controls, the higher incidence of mammary cancer is noticeable. This point cannot be stressed, however, because of the small number of female controls.

The difference in the incidence of lung adenoma is somewhat suggestive. One may perhaps assume, in the light of the work done by Shimkin and Leiter and by Shimkin and Lorenz (*3*), that the mice absorbed out of the smegma a substance of a certain tumor-forming power.

There is nothing to indicate the possible nature of the supposed carcinogenic factor in smegma. It can hardly be just a result of decomposition in stagnating skin products. If this were the case, one should expect cancers in, for example, the umbilicus of obese people or in dermoid and epidermoid cysts.

The chemical composition of smegma has been studied very little and not recently. For decades histologists have disagreed on the question of whether the glans and the inner layer of prepuce contain sebaceous glands and in what numbers. According to Stieve (*4*), only occasional glands occur, and these play no part in the formation of smegma which, in his opinion, is a product of skin desquamation.

Provided our results can be duplicated and improved, this may be the first experimental production of cancer by external application of an external product of the animal body. There is, however, no way of knowing how far the skin epithelium was intact at the time the tumors developed.

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IN THE LABORATORY

A Simple Laboratory Apparatus for the Demonstration of Cardiac Ballistics

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While the output of the heart is usually considered at some length in the physiology textbook and in the classroom, there appears to be no simple laboratory experiment in common use through which some of the more outstanding features of cardiac output may be demonstrated to the student. Dilution and foreign gas methods of estimating cardiac output and the direct Fick procedure, because of complexity and other reasons, are seldom practicable in the teaching laboratory. Of the secondary methods which may be used, the ballistocardiograph is of great value in studying changes in heart output. However, because of its rather complicated structure and certain technical difficulties, this device is found in relatively few laboratories.

In the belief that a less elaborate method of recording cardiac ballistics might be of interest, the description of a simple ballistocardiograph is submitted. The parts required for its assembly are readily available and include an ordinary bath scale, a writing lever, and a kymograph. The arrangement is shown in Fig. 1.

The use of a personal scale in the apparatus stems from the observation that the indicators of certain types of such machines show small rhythmic deflections corresponding to the pulse of the subject being weighed.[1] Because of its small size and construction, this type is the most convenient for the present purpose. While several varieties of these scales are available, the Detecto scale,[2] which registers by means of a vertically placed revolving drum, is best suited. When the subject stands upon the platform, the scale mechanism reaches equilibrium rapidly, but the drum does not remain completely stationary. There occurs a series of slight but noticeable oscillations which are found to correspond in frequency to the pulse rate. These oscillations are, in fact, produced by the recoil of the body from the ejection of blood from the heart and the passage of blood through the aorta.

The writing lever is cut from a thin sheet of celluloid in the shape indicated. The movements of the drum, A, are transmitted to the lever by means of a stiff wire, B, which engages in a small hole at C. The location of the fulcrum and the length of the writing arm are determined by the degree of amplification desired.

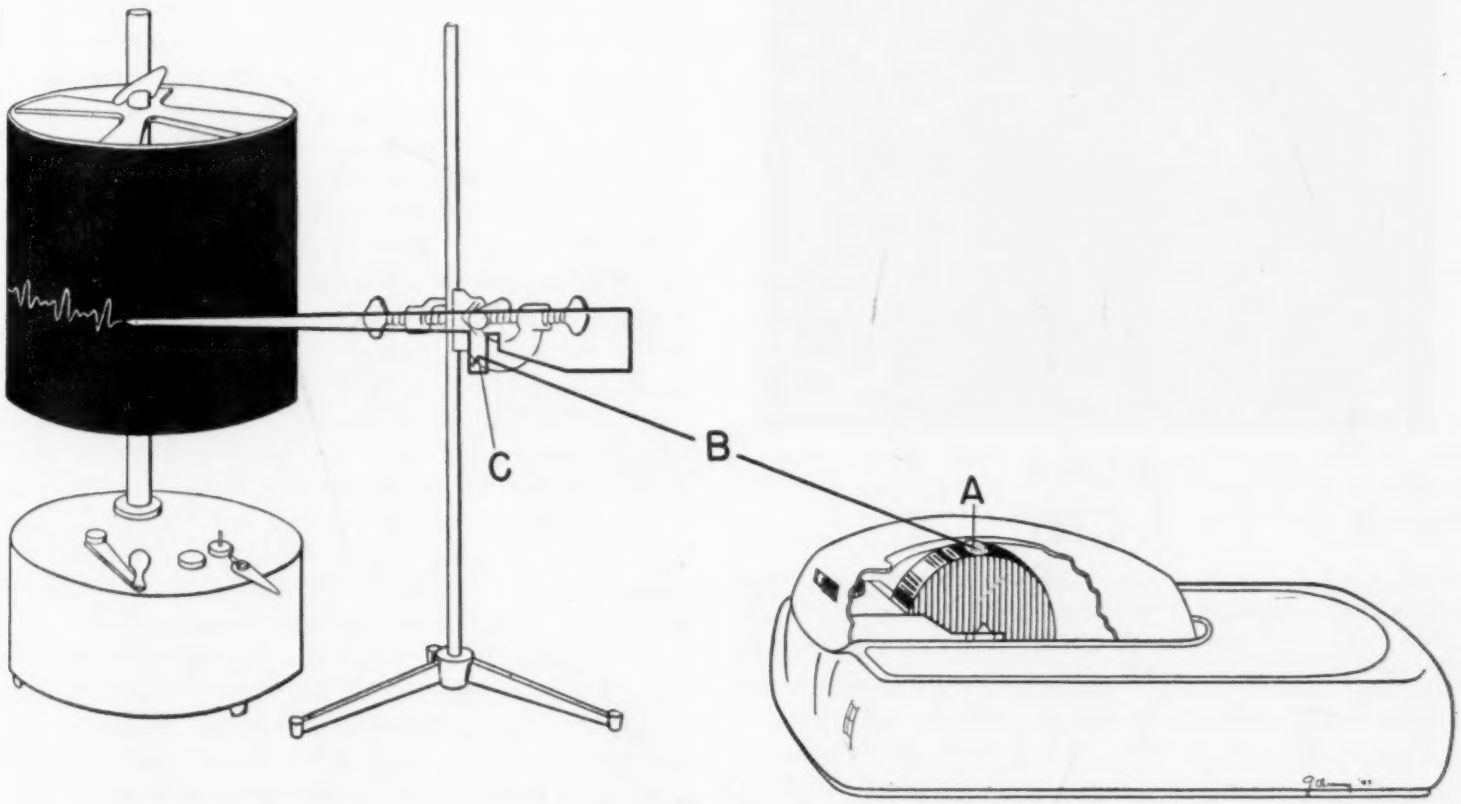

FIG. 1.

The plastic cover of the drum is removed. With the subject standing quietly upon the platform, the wire is attached to the lever at one end and to the drum at the other. The latter is

[1] A similar observation was made 70 years ago on a different type of scale by Gordon (*J. Anat. Physiol.*, 1877, **11**, 533), who recorded these deflections and thus made the first ballistocardiographic tracings.

[2] Detecto Scales, Inc., 1 Main Street, Brooklyn 1, New York.

conveniently done by sticking the flattened end of the wire to the drum's surface with a bit of Tackiwax.[3] Finally, the kymograph drum is brought up to the writing point so that light contact is made. The kymograph is run at a speed which shows the characteristic ballistic waves to best advantage.

Fig. 2(A) shows a typical ballistic wave pattern which was obtained with the apparatus described, the waves being indicated by the customary letters. In some records the L, M, and N waves are indistinct. There is some difference of opinion as to whether these are only a result of after-vibrations or are caused by forced movements. Nevertheless, the first and more important waves appear distinctly. While not intended to give quantitative information concerning the cardiac output, this ballistocardiograph does register changes in that value and may be used to demonstrate to the student some of the factors known to influence the output of the heart. Suggested demonstrations are the effects of exercise, normal and sustained respiration, and drugs upon cardiac output. Fig. 2 (B, C, and D) shows records obtained before and after moderate exercise.

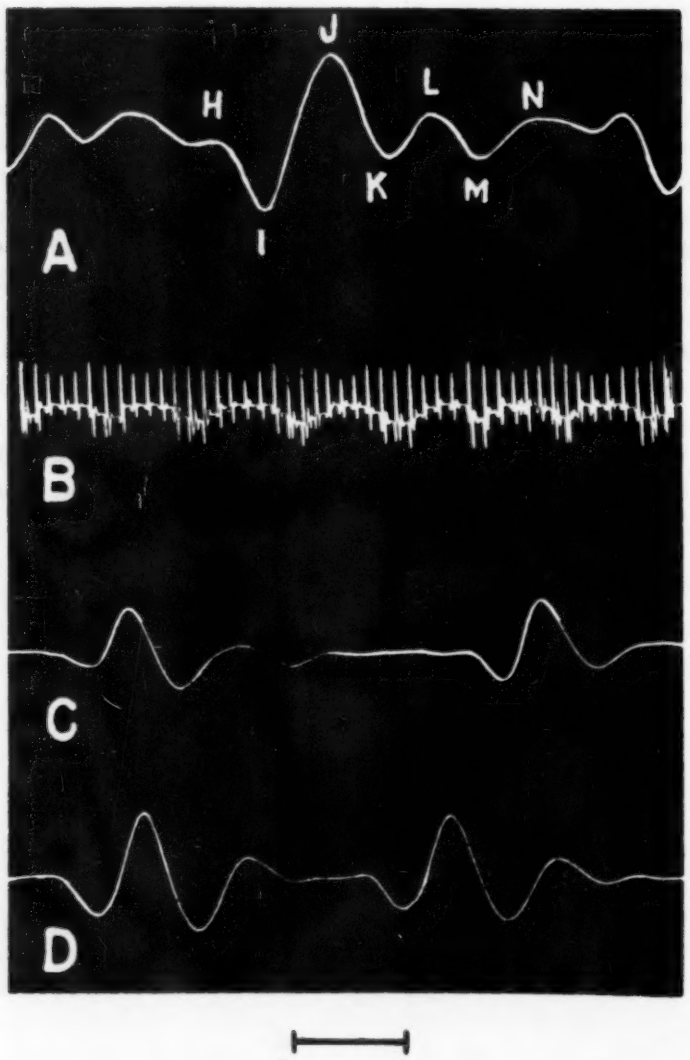

FIG. 2. Tracings obtained with the ballistocardiograph: A, typical pattern with the waves indicated by the customary letters; B, record obtained prior to exercise, with kymograph set at slow speed to show the respiratory waves to best advantage; C, continuation of B with kymograph set at higher speed; D, record of the subject in B and C after moderate exercise. (Note increased I-J distance.)

This ballistocardiograph produces the characteristic pattern of ballistic waves obtained with other, more elaborate instruments. Since the apparatus is inexpensive, is easily assembled, and does not require special training for its successful operation, it may be found useful as a teaching aid in the physiology laboratory.

[3] Cenco-softseal Tackiwax, Central Scientific Company, Chicago, Illinois.

Control of *Nosema* Disease of Potato Tuber Worm, a Host Used in the Mass Production of *Macrocentrus ancylivorus*

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In several laboratories where *Macrocentrus ancylivorus* Roh., an important parasite of the oriental fruit moth, *Grapholitha molesta* (Busck), is being propagated on the potato tuber worm, *Gnorimoschema operculella* (Zell.), serious losses in the production of parasites have been caused by a *Nosema*[1] disease which infects the tuber worm and the parasites reared from it. Infections of 80 per cent or more in the host stocks are not uncommon, and a large portion of the parasites that are produced on even moderately diseased host material may become infected. Diseased parasites are undesirable because they are short-lived and have lowered reproduction capacities.

Nosema disease in potato tuber worm stocks can be controlled by segregating a few pairs of disease-free moths and breeding them through successive generations in a location free of the disease. Although effective, this method is time consuming, and there is also the constant danger of reinfection.

A practical method of controlling *Nosema* disease was developed from suggestions of the junior author. This method takes advantage of the fact that the disease has been found to be transmitted through the host egg. Eggs of the potato tuber worm on paper sheets, which were obtained by the method described by Marvin (*1*), were placed in a water-tight metal envelope and immersed in a hot-water bath at 47°C. for 20 minutes. It was found that the eggs must be heated before being incubated. This treatment proved to be highly successful, reducing infections in the host stocks that developed from the treated eggs, and in the parasites reared from them, by 75 to 90 per cent. In one test the average incidence of *Nosema* disease in the parasites produced in eight trays that had been stocked with heat-treated eggs was only 2 per cent, as compared with 15 per cent in the parasites produced in four trays stocked with untreated eggs. All the eggs used in this test were from stocks that had received heat treatment in preceding generations. In concurrent tests the incidence of the disease was 44 per cent in parasites reared on host stocks, the eggs of which had not received heat treatments in preceding generations. In eggs that were heat treated after being incubated until nearly ready to hatch, only slight reduction in *Nosema* resulted. In experimental series in which complete

[1] Determined by R. R. Kudo, University of Illinois, Urbana.

production records were kept, the heat treatment that was used did not affect the viability of potato tuber worm eggs or lower the production of breeding stocks of this host insect.

This method for controlling *Nosema* disease lends itself well to the mass-production routine, and with little additional work it insures the production of parasites that are comparatively free of the disease.

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A Single Flashlight Source for Ultracentrifuge Research

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Most of the optical ultracentrifuge observations reported in the literature have been made with the aid of continuous light sources which yield sweep images (*8*). While these are, as a rule, satisfactory for the analysis of sedimenting boundaries and the computation of sedimentation constants and molecular weights, such records give no information on the actual appearance of the sedimenting material. All events occurring at the same latitude of the ultracentrifuge cell are integrated into a continuous streak or sweep across the field of observation. The application of refractive index gradient or schlieren methods to ultracentrifugal problems in conjunction with continuous light sources cannot be expected to reveal local disturbances, e.g. convection or streaming phenomena, existing conceivably in some regions of the sedimenting system.

Bjoernstahl (*2*) has synchronized a light source with the rotation of the rotor of the oil turbine ultracentrifuge to prevent stray light from reaching the photographic plate. Harvey and Loomis (*5*), in their centrifuge microscope, have employed first a stroboscopic and, later on, a semistroboscopic method of illumination for the study of small objects during rotation. A similar device has been suggested by Pickels (*6*) for use with a spinning top. In the course of development of a simple high-speed centrifuge with a plastic rotor (*7*), one of us (K. G. S.) employed a mechanical switch and a General Radio Strobotak light source with promising result. However, the flashing time of the Strobotak lamp amounts to about 1/30,000 second—long enough to cause blurring of the microscopic images even at moderate centrifugal speeds. A preliminary discussion of the problem with Prof. H. Edgerton, of Massachusetts Institute of Technology, led to the conclusion that the recording of images, free of noticeable blurring, would require an illumination time of the order of 1/1,000,000 second when making peripheral observations at ultracentrifugal speeds.

The problem, then, resolves itself into the need for a suitable flash source of high intensity and a synchronizing arrangement which will "trigger" the flash at the instant when the centrifuge cell is aligned with the camera or microscope.

[1] The kind advice of Prof. W. MacLean, of this Institute, and Dr. F. N. Barnes, of General Electric Company, is gratefully acknowledged.

The ultracentrifuge[2] used in the present experiments has a vertical lucite rotor, 6 inches in diameter. It is powered by a special electric motor, rated at 35,000 r.p.m. without load, which imparts to the plastic rotor a maximum speed of 21,000 r.p.m. through a flexible shaft, provided the rotor chamber is partially evacuated to reduce air friction.

For general information on flash photography, reference is made to the monograph of Edgerton and Killian (*4*). Whereas Edgerton, *et al.* (*3*) employed a special gaseous discharge tube with three electrodes, a General Electric mercury burner of the H-6 type was used in the present experiments. This light source has previously been employed by Barnes and Bellinger (*1*) in their studies of air-flow phenomena. The basic flash circuit, developed by these authors, was kindly placed at our disposal by N. F. Barnes. A transformer and a rectifier supply about 2,000 volts direct current to a 2-microfarad capacitor which, in turn, discharges through the H-6 lamp. Instead of a manual switch, a thyratron tube was used in the discharge circuit for the control of flashing rate. For triggering and timing the discharge, the light of an automobile headlight lamp is conducted through a plastic strip to the periphery of the porthole in the centrifuge casing. On the

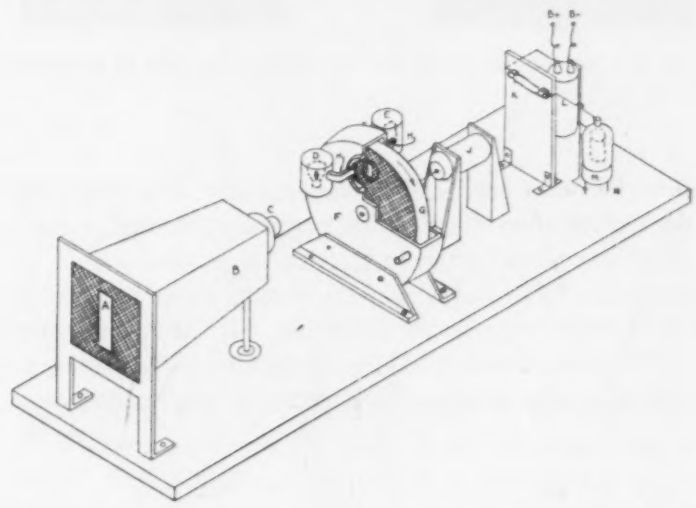

FIG. 1. Experimental arrangement: A, photographic image; B, camera; C, lens; D, synchronizing light source; E, photoelectric cell; F, centrifuge housing; G, plastic rotor with fluid cell; H, transparent plastic strips; J, electric motor; K, B-H-6 mercury lamp; L, 2-microfarad condenser; M, thyratron; N, control grid.

opposite side of the rotor a similar plastic strip conducts the light signal to a vacuum photocell. As the transparent sector of the analytical fluid cell passes through the region of the porthole, the light from the source strikes the photocell cathode. The resulting impulse is amplified, squared, and further differentiated by a RC network arrangement. It was found convenient to employ the trailing rather than the leading edge of the cell sector for the initiation of the flash. The amplified impulse is applied to the thyratron tube in the flash tube circuit, which is so arranged that the discharge through the H-6 source occurs precisely at the instant when the cell is in the center of the porthole and thus aligned with the axis of the photographic system. The camera is equipped with a 5-inch focal length lens. For observation by the schlieren method this system is augmented by a schlieren lens and a horizontal knife edge in front of the camera lens, which is adjustable in the vertical direction. The experimental arrangement is shown schematically in Fig. 1.

[2] This was built by the Development Division of the Fisher Scientific Company, Pittsburgh, in cooperation with one of the authors.

The results obtainable with this arrangement are illustrated in Fig. 2a, which represents the photograph of a stationary ultracentrifuge cell filled with water so as to leave a small air space, and in Fig. 2b, a flash image of the same cell, recorded by a single discharge at approximately 10,000 r.p.m. The air-water meniscus, which is curved in the stationary

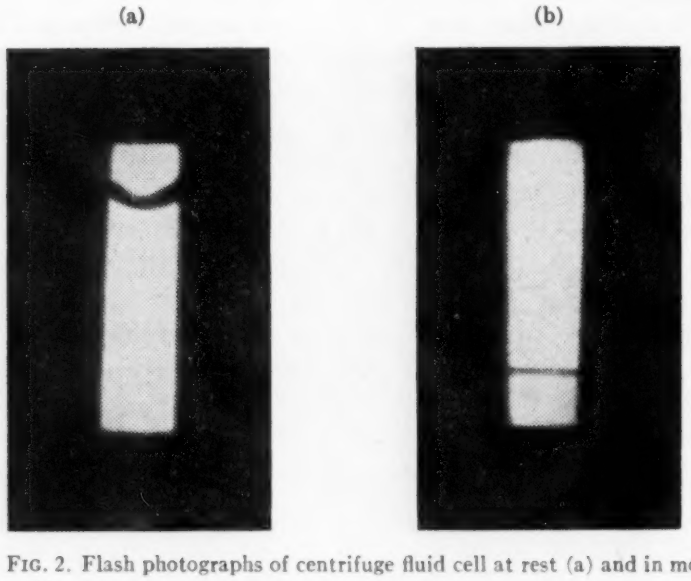

FIG. 2. Flash photographs of centrifuge fluid cell at rest (a) and in motion (b).

picture, becomes practically a straight line. The slight blur at the trailing edge of the cell sector image is probably due to an afterglow phenomenon in the discharge tube.

Images of macroscopic objects during flight may be recorded without appreciable distortion. Fig. 3a is the picture of a stationary, star-shaped object which was attached to the outside of a clear plastic plug inserted in the opaque rotor.

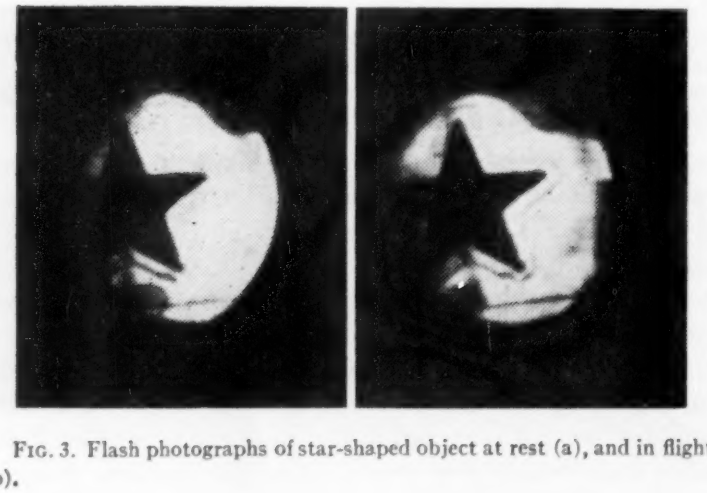

FIG. 3. Flash photographs of star-shaped object at rest (a), and in flight (b).

Fig. 3b represents the image of the same object, photographed with a single flash during rotation at about 4,000 r.p.m. The sedimenting boundary of tobacco mosaic virus protein has been photographed by the schlieren method with the aid of single light flashes.

It is evident that the arrangement here outlined lends itself, in principle, to other applications, e.g. the photomicrography of small objects, such as individual cells, and to studies of photoelastic stress patterns in polarized light. A full report of this work will be published elsewhere.

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An Apparatus for the Determination of the Tensile Strength of Healing Wounds

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The role of nutrition in wound healing has been the subject of few quantitative studies. Harvey and Howes, in their studies on the effect of nutritional state on the rate of healing of wounds, used tensile strength as a measure of repair (*1, 2*).

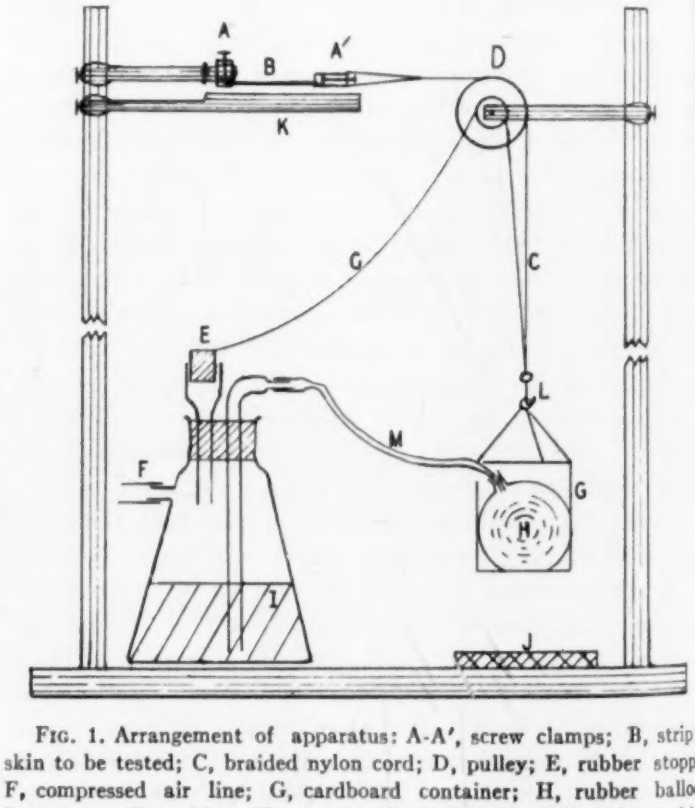

FIG. 1. Arrangement of apparatus: A-A', screw clamps; B, strip of skin to be tested; C, braided nylon cord; D, pulley; E, rubber stopper; F, compressed air line; G, cardboard container; H, rubber balloon; I, mercury; J, cushion; K, support plate; L, hook; M, rubber tubing.

In the course of our work on the role of protein nutrition in wound healing, a simple, semiautomatic apparatus for measuring the breaking strength of skin wounds was devised.

[1] The authors wish to thank Miss Lois H. Henneberger and Miss Mary A. Lord for their technical assistance.

The apparatus allows a uniform rate of loading, can be constructed easily with ordinary laboratory equipment, and is simple and rapid in operation.

In order to determine the strength of a wound, a 0.50-cm. strip of skin is cut out at right angles to the wound. The ends of the strip are fastened to clamps A-A′, the support plate K facilitating manipulation of the strip. The apparatus is arranged as shown in Fig. 1, and compressed air is turned on at F, driving mercury into the balloon, H, at 900–1,100 grams/minute. When the limit of strength of the skin strip is attained, it breaks and container G falls, pulling out stopper E and automatically halting the flow of mercury. Container G is then weighed without detaching from the apparatus.

The reproducibility of the results obtained is indicated by determinations of the breaking strength of similar 0.50-cm. strips of freshly dissected, unwounded rat skin. Determination on 10 rats (135–190 grams in weight) gave values ranging from 1,410 to 1,990 grams; the average value was 1,710 grams, and the average deviation, 170 grams.

An experiment demonstrating the possibilities of this approach to the study of wound healing was set up as follows:

Young male rats (140–160 grams) were divided into two groups and fed ad libitum diets containing 6 per cent and 22 per cent casein. The percentage composition of the diet for each group is given below:

	Group I	Group II
Casein	6	22
Dextrose	73	57
Salt mixture No. II (SMA)	4	4
Crisco	15	15
Cod liver oil	2	2

The rats were given a daily supplement of thiamine, pyridoxine, riboflavin, calcium pantothenate, and choline chloride and were supplemented weekly with vitamins A, D, and E.

After 7 days on diet, the rats were anesthetized with nembutal and ether, and the hair in the area of the shoulder blades removed with a pair of clippers. A slit wound (approximately 1 cm. in length) was made longitudinally through the entire thickness of the skin with a scalpel. The edges of the wound were pressed together, and a strip of adhesive tape applied directly to the wound. The edges of the tape were cemented to the skin with a methacrylate polymer mixture consisting of: hydroabietyl alcohol, 20 grams; dibutyl phthalate, 15 grams; isobutyl methacrylate polymer, 50 grams; isobutyl-N butyl methacrylate interpolymer, 40 grams; and toluene, 150 ml.[2]

The hind paws of the rat were incased in test-tube ends filled with plaster of Paris in order to prevent the animal from scratching at the wound. (Further experience has shown that this precaution is unnecessary.) The dressing adhered for approximately 10 days, after which the wound had healed sufficiently to render protection unnecessary. With this technique close proximation of the wound edges was obtained; infection and scabbing rarely occurred.

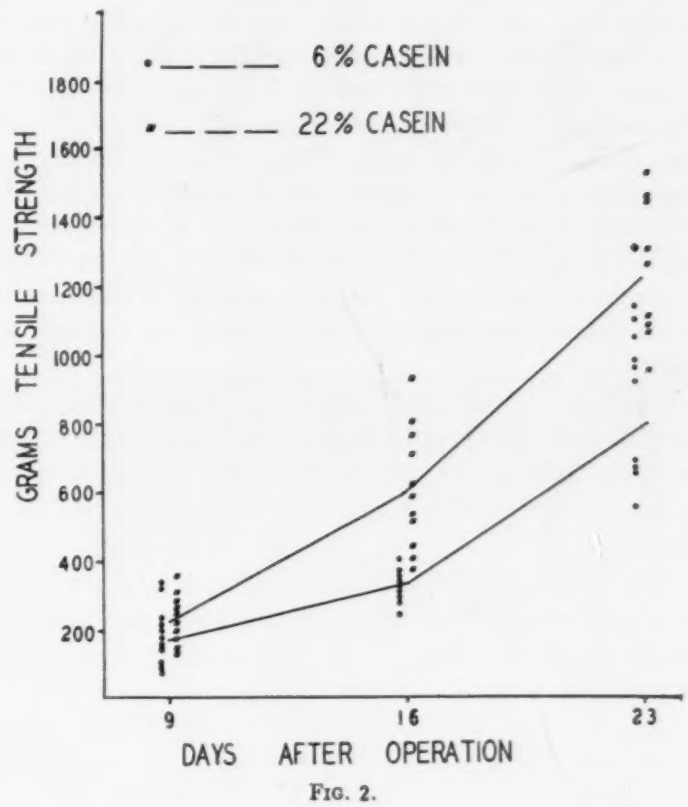

FIG. 2.

After 9, 16, and 23 days, the animals were sacrificed and wound strength determined (Fig. 2). The average error and calculations of significance of each group of rats are given in Table 1.

The data shown in Fig. 2 and Table 1 demonstrate the unfavorable effect of suboptimal dietary protein level on the rate of healing of skin wounds in the rat. This has been confirmed by several repeat experiments using the same technique and apparatus. The data serve to confirm the report of Harvey and Howes on the beneficial effect of high protein diets on the healing of experimental wounds.

TABLE 1

RELATIONSHIP BETWEEN DIETARY PROTEIN LEVEL AND BREAKING STRENGTH OF SKIN WOUNDS

	6% Casein		22% Casein		Critical ratio (*3*) $\left(\frac{x}{\sigma}\right)$	Probability of significance (*3*)
9 days	10 rats	178 ± 67 grams	10 rats	229 ± 47 grams	1.5	6 to 1
16 "	9 "	314 ± 36 "	11 "	602 ± 135 "	5.2	2×10^{3} to 1
23 "	11 "	800 ± 223 "	9 "	1,222 ± 264 "	4.0	1.5×10^{4} to 1

[2] The methacrylate polymers were supplied by E. I. du Pont de Nemours and Company, Wilmington, Delaware.

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While not professing to be a systematic development of the principles of analytic dynamics, this useful booklet presents an interesting approach to a set of problems which are usually regarded as difficult by the student. It selects for consideration the motion of bodies in accelerated reference systems and derives from Newton's laws or Lagrange's equations the basic laws of motion, which are applied to specific instances. The treatment includes the general motion of a rigid body, motion relative to the rotating earth, the motion of a top, and Euler's dynamical equations. One chapter is devoted to the dynamics of an inextensible flexible chain; it excels in elegance and clarity.

Throughout the book, problems are chosen for their illustrative value and mathematical tractability, and without reference to their practical importance. The contents are meant to be supplementary to the standard treatises on dynamics.

The book should prove valuable in the hands of a teacher of graduate courses in dynamics who wishes to enliven the treatment of the subject by interesting and unorthodox examples.

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